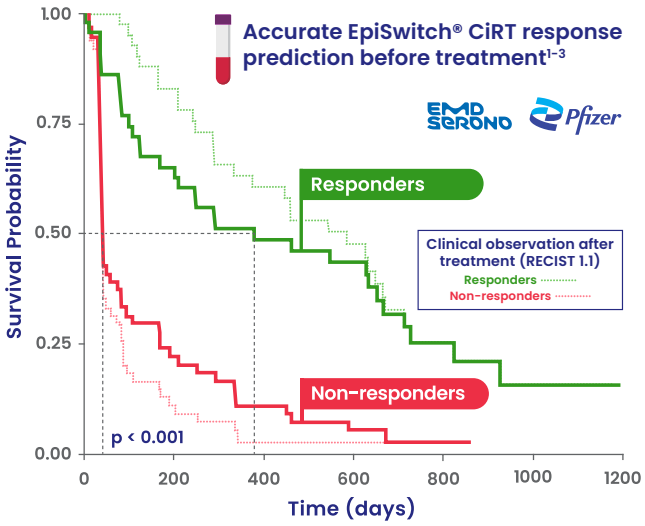
EpiSwitch® CiRT
Checkpoint inhibitor Response Test

CiRT Customer Service
+44 (0)1865 504 932 (UK)
+1 888-236-8896 (US)

Learn more at
myCiRT.com

Accurately predict clinical response to immune checkpoint inhibitor (ICI) therapy from blood

- Blood test detects epigenetic markers to **accurately identify which patients will respond to an ICI**
- Supports **first-line treatment planning, navigating adverse events,** and identifying ICI candidates in patients where other options have been exhausted
- **Run before or during ICI treatment,** and anytime before, during or after basic standard of care
- CiRT validated **with widely used anti-PD-(L)1 ICIs** Pembrolizumab, Atezolizumab, Durvalumab, Nivolumab, Avelumab across **14+ broad oncological indications**[1] including breast, lung, prostate, stomach, liver (HCC), kidney (RCC), pancreas, bladder, head & neck, bile duct, cervix, vulva, colon, brain



EpiSwitch CiRT results are easy to interpret

EpiSwitch® CiRT Response Report

Personalized Immune Health 3D-Genetic Profile

Patient Name	Date of Birth
Peterson, Janette	22-DEC-1975

EpiSwitch CiRT Response Profile

Your Response Level

Low Likelihood | **High Likelihood**

The **EpiSwitch Checkpoint inhibitor Response Test (CiRT)** result for this specimen is in the **High Likelihood of Response** range to an Immune Checkpoint Inhibitor (ICI) therapy. Individuals in the group have a greater chance of benefiting from an ICI agent. This result should be considered along with other clinical features for interpretation by a licensed medical professional.

Patient Information

Gender	Female
Medical Record #	c14456d0
Report #	CiRT0254

Physician Release

Physician Name	Christopher Smith, MD, MS
Facility Name	XXX-XXX-XXX-XXX
Address	[Address line] [City], [State] [Zip]
Phone	811-555-4210
Account Ref	FL

Specimen Information

Report Date	28-FEB-2021
Receipt Date	28-FEB-2021
Collection Date	20-FEB-2021
Specimen Type	WB EDTA K3
Specimen ID	D000097422

EpiSwitch Checkpoint inhibitor Response Test Description

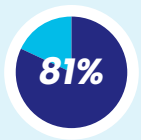
Intended Use: Checkpoint inhibitor Response Test (CiRT) is a blood test that evaluates DNA conformational structures in the immune cells to assess the likelihood of response to immune checkpoint inhibitor (ICI) therapy targeting PD-L1 (Atezolizumab, Avelumab, Duralumab) and PD-1 (Pembrolizumab). The results are not specific to ICI agent or to type of tumor. The test is intended to provide supplemental information to cancer treatment professionals on the overall clinical picture. It should not be used as the sole data point in treatment decisions.

EpiSwitch CiRT Response Test is a quantitative laboratory developed blood test to assess the likelihood of response to an ICI therapy. The test evaluates eight (8) DNA regulatory (epigenetic) markers called chromatin-conformational signatures (CCS) and stratifies patients based on their probability of responding to an ICI. The test may be run at any stage of treatment, including post-initiation of an ICI.

References

1. Hunter, E., Salter, M., et al., (2023). Development and Validation of Blood-Based Predictive Biomarkers for Response to PD-1/PD-L1 Checkpoint Inhibitors: Evidence of a Universal Systemic Core of 3D Immunogenetic Profiling across Multiple Oncological Indications. Cancers. 2023; 15(10):2696. https://doi.org/10.3390/cancers15102696.

ACCURACY[1]



SPECIFICITY

SENSITIVITY

NEGATIVE PREDICTIVE VALUE

1. Hunter, E. et al. (2023) Cancers 2023. doi.org/10.3390/cancers15102696

Oxford BioDynamics

Interpretation of the CiRT result

High Likelihood of response

EpiSwitch CiRT Response Profile

Your Response Level

Low Probability | **High Probability**

Low Likelihood of response

EpiSwitch CiRT Response Profile

Your Response Level

Low Probability | High Probability

TREATMENT PLANNING

- Good candidate for ICI therapy
- Likely candidate for neo-adjuvant treatment before surgery
- Consider for ICI monotherapy to avoid toxicity related to BSC
- Strong indication that patient will not respond to ICI therapy
- Consider more aggressive treatment; 3 or 4 agents + the ICI
- ***Option:*** Proceed with limited cycles (3-5) and evaluate for response – stop if response/benefit is not observed

ADDRESSING IMMUNE-RELATED ADVERSE EVENTS

- Reinforces that patient should be reset and placed back on the ICI
- ***Moderate Events:*** some may not be life threatening, but could impact quality of life – this result indicates that a patient's symptoms should be managed, and the patient remain on ICI
- Patients should be taken off ICI and symptoms managed; they should not be a candidate for return to treatment
- ***Moderate Events:*** if therapy is impacting the patient's quality of life, then consider removing the patient from ICI and seek alternate treatment

NEGATIVE IHC OR TMB CONTRAINDICATION

- High likelihood that the patient will respond to an ICI regardless of other test results, like IHC and TMB
- CiRT predicts the host's response, not the tumor's
- Taken in conjunction with standard testing, the patient is not a likely candidate for ICI treatment – consider alternatives

PSEUDO-PROGRESSION

- ***Pseudo-progression RULE IN:*** confirmation by CiRT that pseudo-progression is being observed; continuation of ICI therapy will likely benefit the patient
- ***Pseudo-progression RULE OUT:*** Confirmation that this is not pseudo-, but actual disease progression; the treatment plan should potentially be reconsidered

Get Started with EpiSwitch® CiRT

1. Pre-authorise via the Bupa provider services team on 0345 755 3333. Send the completed requisition and patient consent forms by Egress encrypted email to **CiRT.TEST@myOBDX.com**, or by uploading them at **www.obdx.co/upload**.
2. Send a small blood sample (2 mL) to a CiRT testing lab using our Collection Kit. The test analyzes eight epigenetic biomarkers to predict a patient's response to an ICI.
3. Within a few days of receiving a sample, the CiRT result will be securely sent to the ordering physician.

Rapid results in days

Scan to download your forms at **myCiRT.com**

Publications about CiRT

1. Hunter, E., Salter, M., et al. (2023). **Development and Validation of Blood-Based Predictive Biomarkers for Response to PD-1/PD-L1 Checkpoint Inhibitors: Evidence of a Universal Systemic Core of 3D Immunogenetic Profiling Across Multiple Oncological Indications.** *Cancers 2023;* 15(10):2696 https://obdx.co/cirt01

2. Shah, P., Hunter, E., et al. (2019). **Development and Validation of Baseline Predictive Biomarkers for Response to Avelumab In Second-Line (2L) Non-Small Cell Lung Cancer (NSCLC) Using Episwitch Epigenetic Profiling.** SITC, J. *Immunotherapy Cancer* 7(282) P142. https://obdx.co/cirt03
Co-published by authors from Oxford BioDynamics, EMD Serono, Pfizer, and the Mayo Clinic

3. Shah, P., Hunter, E., et al. (2019). **Development And Validation Of Baseline Predictive Biomarkers for Response to Immuno-Checkpoint Treatments in the Context of Multi-Line And Multi-Therapy Cohorts Using Episwitch Epigenetic Profiling.** SITC, J. *Immunotherapy Cancer* 7(282) P143. https://obdx.co/cirt04
Co-published by authors from Oxford BioDynamics, EMD Serono, Pfizer, and the Mayo Clinic

4. **Genomic Biomarkers in Peripheral Blood From Patients Enrolled in the Javelin Bladder 100 Trial of Avelumab.** *Annals of Oncology* | SEP 10, 2022. https://obdx.co/cirt02

Oxford BioDynamics

EpiSwitch® CiRT Response Test Requisition Form (UK)

For Lab Use	For Lab Use
Order #	Kit Barcode ID #

To order, submit the completed requisition and patient consent forms by fax to 01865 504691, or by Egress encrypted email to CiRT.test@myOBDX.com, or upload at www.obdx.co/upload. For any questions, please email CiRT.test@myOBDX.com or call 01865 504932.

TESTING MAY BE DELAYED IF REQUIRED FIELDS ARE NOT PROVIDED

Patient Information

First Name | MI | Last Name | NHS Number # (optional) | DOB (Day Month Year) | Gender: (optional) ◯ F ◯ M

Address | City | Postal Code | Country | Primary Phone

Patient Diagnosis & History

Diagnosis

Additional Case information (optional)

Treating Physician Information

Please provide best contact information for case follow-up

Facility or Practice Name | Treating Physician (full legal name) | GMC Registration Number

Facility/Practice Address | City | Postal Code | Country | Phone

Oxford BioDynamics Account # (optional) | Email | Fax (optional)

Additional Physician to be Copied (optional) | Facility Name (optional) | Email (optional) | Fax (optional)

Test Menu and Specimen Collection

Test	*Description*	*Accepted Specimen Type*	*Minimum Volume Required*
◯ EpiSwitch CiRT Response Test	Predictive test that identifies a cancer patient's likely response to an Immune Checkpoint Inhibitor (Blockade) Therapy.	Whole blood, EDTA Tube	3 mL

Intended Use and Technical Information

Intended Use: Checkpoint inhibitor Response Test (CiRT) is a blood test that evaluates DNA conformational structures in the immune cells to assess the likelihood of response to immune checkpoint inhibitor (ICI) therapy targeting PD-L1 (Atezolizumab, Avelumab, Duralumab) and PD-1 (Pembrolizumab). The results are not specific to ICI agent or to type of tumor. The test is intended to provide supplemental information to cancer treatment professionals on the overall clinical picture. It should not be used as the sole data point in treatment decisions.

EpiSwitch CiRT Response Test is a laboratory developed test (LDT). It has not been reviewed or cleared by the US Food and Drug Administration. The laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity clinical testing. Decisions regarding patient care and treatment should not be solely based on a single test such as this test, rather, on the independent medical judgment of the treating physician taking into consideration all available information concerning the patient's conditions, including other clinical tests, in accordance with the standard of care in each healthcare setting.

Billing Information

Name (the contact for billing or insurance cover) | Email | Phone

Address | City | Postal Code | Country

Test Authorization and Physician Signature

The undersigned certifies that he/she is licensed to order the test(s) listed above and that such test(s) are medically necessary for the care/treatment of this patient.

Treating Physician Signature | Printed Name *(full legal name)* | Date (Day Month Year)

EpiSwitch® CiRT *is the only test*

that predicts how a patient will respond to immune checkpoint inhibitor (ICI) therapies

Order the CiRT test

The Checkpoint inhibitor Response Test (CiRT) can only be ordered by a physician using the CiRT Requisition Form

- Download the **Requisition Form** at **https://myCiRT.co/order-test**

Complete the Requisition Form

Work with your physician to complete the **Requisition and Patient Consent forms**

- Your physician will submit the completed forms by: fax to **01865 504691**, Egress encrypted email to **CiRT.test@myOBDX.com**, or upload to **www.obdx.co/upload**
- For any questions, please email **CiRT.test@myOBDX.com** or call **01865 504932**

Provide a small blood sample

- CiRT Customer Service will send you or your physician a Specimen Submission Kit to ship your blood sample
- Coordinate with your provider to schedule a blood draw

Receive your CiRT test result

Within 5 days of receiving the sample, your Checkpoint inhibitor Response Report will be sent to your physician

- Navigate the toughest challenges of immunotherapy by knowing your likelihood of response to ICI therapy

Questions? Email CiRT Customer Service at **CiRT.test@myOBDX.com**

EpiSwitch® CiRT
Checkpoint inhibitor Response Test

Learn more at
www.myCiRT.com

EpiSwitch® Patient Consent Form (UK)

Service ordered:

○ **EpiSwitch® CiRT** (Checkpoint inhibitor Response Test)
Predicts your likely response to Immune Checkpoint Inhibitor (ICI) cancer therapy

○ **EpiSwitch® PSE** (EpiSwitch Prostate Screening Test)
Predicts a patient's current risk of prostate cancer from blood

Patient Information and Declaration of Consent to Processing of Personal Data

Your physician has recommended analysing your blood to perform the EpiSwitch test marked above ("Service").

The Service is provided by Oxford BioDynamics ("OBD") in conjunction with a 3rd-party laboratory as set out below:

- The Service is offered in your country by OBD, who is responsible for the processing of any personal data received from you in the context of providing the Service. OBD handles the central coordination and quality of the Service provision in your country and is also responsible for providing customer support.
- To provide the Service, OBD operates a clinical laboratory and also collaborates with a 3rd-party laboratory ("Partner Lab") in the US. Your sample may be sent to the Partner Lab to perform the laboratory services for this test. If so, your personal data will remain in the UK and will not be sent to or stored by the Partner Lab.

This Patient Information and Declaration of Consent ("Patient Consent Form") informs you about the processing of your personal data by your physician and OBD and serves as the basis for obtaining and documenting your consent to the processing of your personal data.

Section 1 – Consent to the Processing of your Personal Data for Providing the Service

Your consent to the processing of your personal data pursuant to Section 1 is required to provide the Service. To give your consent, please provide your signature at the end of this form.

A. Assignment of Sample ID by OBD (Pseudonymisation Process)

OBD will review your physician's order and upon receipt of your sample assign a pseudonymised identifier ("Sample ID") to your case. OBD will make that Sample ID available to the Partner Lab, if they are required to provide the Service. The Sample ID is a unique central identifier of your case that does not reveal your identity but allows the Partner Lab to exchange test results with OBD in pseudonymised form. Under no circumstances will the Partner Lab receive any information to attribute the Sample ID to your person.

B. Laboratory Analysis and Report Creation

To start the provision of the Service, your physician will complete a test requisition form and provide it to OBD. The form must include the following ("TRF Data"): patient information (e.g., name, date of birth, gender, contact information), physician contact information, and billing information. In addition, the physician may provide a unique identification number (such as a National Health Service number) which may be required by your physician to directly identify you and may also provide details of your case history (your diagnosis).

If the Partner Lab performs the services for the test, they will not receive your TRF Data from either OBD or from your physician. The TRF Data will be stored by OBD on systems and applications operated in the UK. As necessary to provide the Service, OBD may engage technical service providers located in the UK and the US for the hosting and operation of its databases, portals, and applications.

OBD will process TRF Data only for the purpose of providing the Service and not for research and scientific purposes.

If the Partner Lab processes the test, the Medical Director ("Partner Doctor") in the US will be granted view-only access to your report to verify and release the final report to OBD, as required for compliance with regulatory requirements. The report will then be transferred to your physician. Other than as necessary to provide the Service, the Partner Lab will not further analyse or process your sample. The 3D-genomic data obtained during the analysis by the Partner Lab will not contain any directly personal identifiable data. For the avoidance of doubt, OBD does not perform genetic sequencing on your DNA/RNA.

For more details about the roles of OBD, the Partner Lab and Partner Doctor in the context of your Service, please contact your physician or OBD at the contact details set out in Section 2.

Pseudonymised data may be transmitted to the Partner Lab in the US, and thus to another country, the laws of which may not provide for the same level of data protection as considered adequate in the UK. This triggers certain risks, including that it may be more difficult to enforce your data protection rights as a data subject and that your pseudonymised personal data may be subject to access requests under applicable US law by public authorities who may have more extensive powers than the authorities in the UK. To ensure that your data are adequately protected as required by UK data protection laws, OBD and the Partner Lab have implemented supplementary measures, including a privacy by design concept that ensures that only data necessary for the processing of the Service will be transferred to the Partner Lab.

C. Central Coordination of Services, Quality of Service Provision and Customer Service by OBD

OBD will manage access to TRF Data and will also track the status of the provision of the Service based on the Sample ID. OBD's processing is for the purpose of central coordination of the Service, ensuring the quality of the Service provision, and handling of customer service requests. To the extent necessary for these purposes, OBD receives the relevant information from the physician (TRF Data) and Partner Lab (test results and information about the status of Service). OBD will ensure by implementing appropriate technical and organisational measures that the Partner Doctor will be granted view-only access to your report to veri fy and release the final report to OBD.

D. Term of Storage and Deletion

OBD will store and retain your data in accordance with the following processes. The TRF Data and report will be archived by OBD for a maximum of 6 years from the date of the release of the report to your physician ("Completion of the Service") and discarded thereafter. Samples will be discarded by the laboratory once no longer required for the Service and at the latest upon Completion of the Service.

-- continued on reverse

| www.myOBDX.com/PSE | Tel: 01865 504932 | Fax: 01865 504691

Section 2 – General Data Protection Information

The following general data protection information applies to all data processing activities described in Section 1.

A. Contact Details

The Data Protection Officer of OBD is your point of contact regarding any questions, suggestions or complaints concerning the processing of your personal data. All requests or complaints must be in writing, addressed to the Data Protection Officer at OBD:

E-mail: privacy@oxfordbiodynamics.com Fax: 01865 504691

Mail: 3140 Rowan Place, John Smith Drive, Oxford Business Park, Oxford, OX4 2WB

B. Security

OBD takes appropriate technical and organisational measures to protect your personal data against accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, personal data transmitted, stored or otherwise processed.

C. Your Rights

You have the right, in accordance with applicable data protection law:

- to request information about the data processed about you, and to obtain a copy of such data (right of access);
- to obtain the rectification of inaccurate data or, taking into account the purposes of the processing, request the completion of incomplete data (right to rectification);
- to obtain the erasure of personal data to the extent one of the grounds provided for by statutory law applies (right to be forgotten);
- to the extent the statutory requirements are fulfilled, to obtain the restriction of processing of your data (right to restriction of processing);
- to the extent the statutory requirements are fulfilled, to receive any personal data you provided to OBD in a structured, commonly used and machine-readable format and to transmit those data to another controller or, where technically feasible, have the data transmitted (right to data portability); and
- not to be subject to an automated individual decision making if the statutory requirements are not fulfilled. Automated individual decision-making is not taking place.

You further have the right to object, on grounds relating to your particular situation and in accordance with applicable law, to any processing of your personal data (right to object). You further have the right to withdraw your consent at any time without affecting the lawfulness of processing based on consent before its withdrawal.

To exercise your rights, please contact your physician. You may also contact OBD through the contact details in Section 2. You further have the right to lodge a complaint with a data protection authority competent for your place of habitual residence or place of the alleged infringement.

Section 3 – Patient Information and Declaration of Consent to the Processing of Personal Data

IMPORTANT: Please provide your consent on two original copies of this document and return one to your physician; the other copy is for your record. Please do not return a copy of this document to OBD.

Consent to Processing of my Personal Data in accordance with Section 1 – I hereby consent to the processing of my personal data, including my health data, as specified in Section 1 for the purpose of providing the requested Service (as indicated at the top of this form), including transfer of my personal data to OBD and potential for visibility to a Partner Doctor in the US. I am aware that I am not obliged to provide this consent, however if my consent is not granted, Service cannot be provided. I may withdraw this consent at any time by contacting my physician or OBD as set out in Section 2. If I withdraw my consent, the Service will be deemed to be terminated and will be stopped at its then current stage.

Patient's signature:	Patient's name (PRINT):	Date (DD-MMM-YYYY)

Patient Agreement of Financial Responsibility

Send by fax to 01865 504691, or by Egress encrypted email to CiRT.test@myOBDX.com, or by uploading them at www.obdx.co/upload. For any questions, please email CiRT.test@myOBDX.com or call 01865 504932

FINANCIAL AGREEMENT

The **EpiSwitch® CiRT** service is a new molecular profiling lab test. By signing this form, I acknowledge that my doctor and I have agreed to proceed with testing. A billing representative from Oxford BioDynamics will be contacting me to obtain payment information. **Furthermore, I understand that my responsibility for these services is provided below and that I may be required to make full payment in advance of testing as payment toward the total charges:**

EpiSwitch® CiRT
£1,950

BILLING INFORMATION

Indicate if you have confirmed that your health insurer will be covering the test

○ Self-pay ○ Bupa ○ Aviva ○ AXA ○ Other insurer _____

_____ _____

Patient Name (Please write clearly) Best Phone Number to Call

_____ _____

Signature of Patient / Legal Representative Date

_____

If signed by legal representative, describe relationship to the patient and authority to act on behalf of the patient