EpiSwitch® CiRT Technical Overview

EpiSwitch CiRT is a quantitative laboratory developed blood test to assess the likelihood of response to an Immune Checkpoint Inhibitor (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.

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 Interpretation: Personalized Immune Health 3D-Genetic Profile

Low Probability | **High Probability**

Low Probability Management Guidance

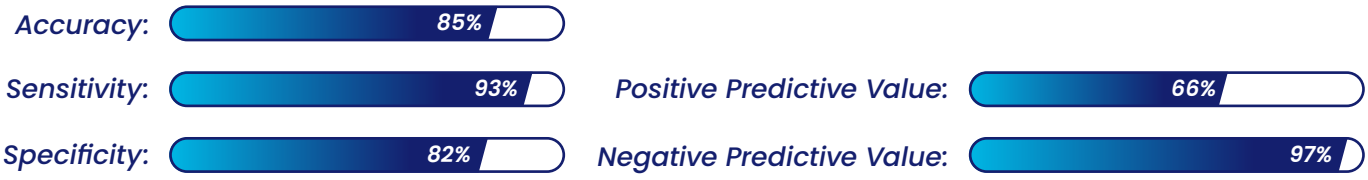
The **EpiSwitch Checkpoint inhibitor Response Test (CiRT)** result for this specimen is in the **Low Likelihood of Response** range to an ICI therapy. This result should be considered along with other clinical features for interpretation by a licensed medical professional.

High Probability Management Guidance

The **EpiSwitch Checkpoint inhibitor Response Test (CiRT)** result for this specimen is in the **High Likelihood of Response** range to an 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.

A Validated Predictive Test to Stratify Individuals Based on Their Likelihood of Response to Immune Checkpoint Inhibitors (ICIs)

EpiSwitch CiRT delivers high sensitivity and specificity for predicting the beneficial use of an ICI agent. The blood test measures eight epigenetic markers to determine the most likely outcome of treatment.



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
2. Hunter, E., Dizfouli, M., et al., (2021). Development and validation of blood-based predictive biomarkers for response to PD-(L)-1 checkpoint inhibitors: evidence of a universal systemic core of 3D immunogenetic profiling across multiple oncological indications. MedRxiv. https://doi.org/10.1101/2021.12.21.21268094.
3. 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://dx.doi.org/10.1186/s40425-019-0763-1. Co-published by authors from Oxford BioDynamics, EMD Serono, Pfizer, and the Mayo Clinic.
4. 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://dx.doi.org/10.1186/s40425-019-0763-1. Co-published by authors from Oxford BioDynamics, EMD Serono, Pfizer, and the Mayo Clinic.

Get Started With EpiSwitch® CiRT

Healthcare Provider & Patient Resources

Your online resource to learn more about EpiSwitch CiRT: **www.mycirt.com**

LEARN MORE by contacting your local EpiSwitch CiRT customer service representative by phoning **888-236-8896** or emailing us at **CiRT.TEST@myOBDX.com**

EpiSwitch CiRT Sample Report

Response Category
Response Category presented as *High Probability* or *Low Probability.*

Test interpretation
Specific to the patient's *Risk Category*, presented as an aid to the physician.

Assay Description
Giving detail into the eight biomarkers that are measured and combined into the single EpiSwitch CiRT score.

EpiSwitch® CiRT Response Report

High Likelihood of Response example

Personalized Immune Health 3D-Genetic Profile

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

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

EpiSwitch CiRT Response Profile

Your Response Level

Low Probability | **High Probability**

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.

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.
2. Hunter, E., Dizfouli, M., et al., (2021). Development and validation of blood-based predictive biomarkers for response to PD-(L)-1 checkpoint inhibitors: evidence of a universal systemic core of 3D immunogenetic profiling across multiple oncological indications. MedRxiv. https://doi.org/10.1101/2021.12.21.21268094.
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Disclaimer: The 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.

This test was performed at NEXT Bio Research Services, LLC, 11601 Ironbridge Rd, Chester, VA 23831 – CLIA #49D2104154.
For questions about the report, email CiRT.TEST@myOBDX.com or call 1.888.236.8896.

Medical Director Signature | Date

CiRT 102-01-01-03

The Benefits of Using EpiSwitch CiRT in Your Clinic

- Personalized insight into ICI therapy response
- Easy to implement
- Impactful actionable guidance