CURESPONSE

KNOW. BEFORE.

An innovative test to optimize the treatment of cancer patients

The cResponse™ test combines the assessment of tumor sensitivity to various oncological treatments with rapid genomic sequencing, enabling selection of the most suitable treatment for each patient individually

Scientific background

Numerous studies have shown that tumors in different individuals show variability and that each cancer patient will respond differently to anticancer drugs.

Each tumor has its own genetic characteristics, which differ among patients. These genetic changes affect the development of the tumor and its response to various treatments. In addition to cancer cells, the tumor environment consists of many other types of cells including immune cells, mast cells, blood vessels, and bacteria. The composition of the tumor environment varies from patient to patient and influences the effectiveness of various oncological drugs.

Tests that solely perform genomic sequencing of the tumor tissue may identify mutations to which specific biological target therapies can be tailored. However, even in situations where a particular actionable mutation has been detected, not all patients will respond to the treatment associated with that mutation, and it is impossible to adequately predict which patients will respond and which will not. In addition, genomic sequencing cannot identify and evaluate the response to various chemotherapies and biological treatments that do not have a specific target mutation.

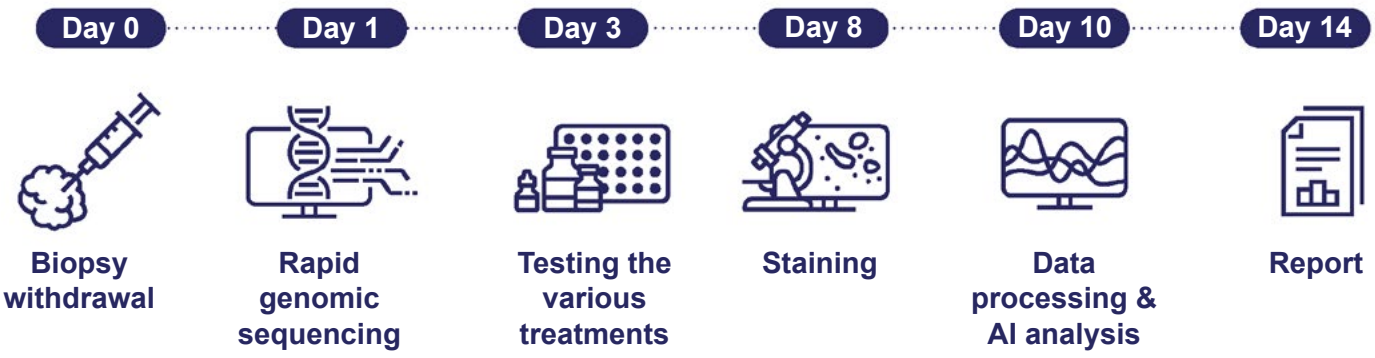
cResponse™ test

The cResponse™ test combines rapid genomic sequencing and the examination of the sensitivity of tumors to various oncological treatments.

The test's innovative technology is based on sampling fresh tumor tissue through biopsy or surgery and growing it under laboratory conditions in a unique manner that preserves the tumor's complex system and its environment over time. Unlike tests that only perform genomic sequencing, the cResponse™ test allows testing the effectiveness of chemotherapy and innovative biological treatments on the tumor tissue, both as a single drug as well as a combination of several drugs. The test prioritizes the various treatments according to their degree of effectiveness in destroying the cancerous cells, that is, the degree of tumor sensitivity to a certain drug.

The test will assist the treating oncologist to choose the most effective and appropriate treatment for each patient and their specific cancer.

Testing procedure



Fresh tumor tissue from surgery or biopsy arrives at Curesponse's laboratory and is cut into sections, each of which is treated with a drug or a different combination of drugs according to the oncologist's request. Drugs targeting actionable mutations identified by genomic sequencing are also added. The list of treatments must be provided before the tumor tissue arrives at the laboratory. Following treatment, the tissue sections undergo histological processing and evaluation by the Company's pathologists, who evaluate the drugs' effectiveness according to various criteria. The information resulting from the pathological evaluation is weighted by a unique algorithm developed by Curesponse and translated into a final score, which reflects the tumor's sensitivity to the tested treatments.

Genes tested by rapid genomic sequencing for tailoring innovative targeted biological treatments

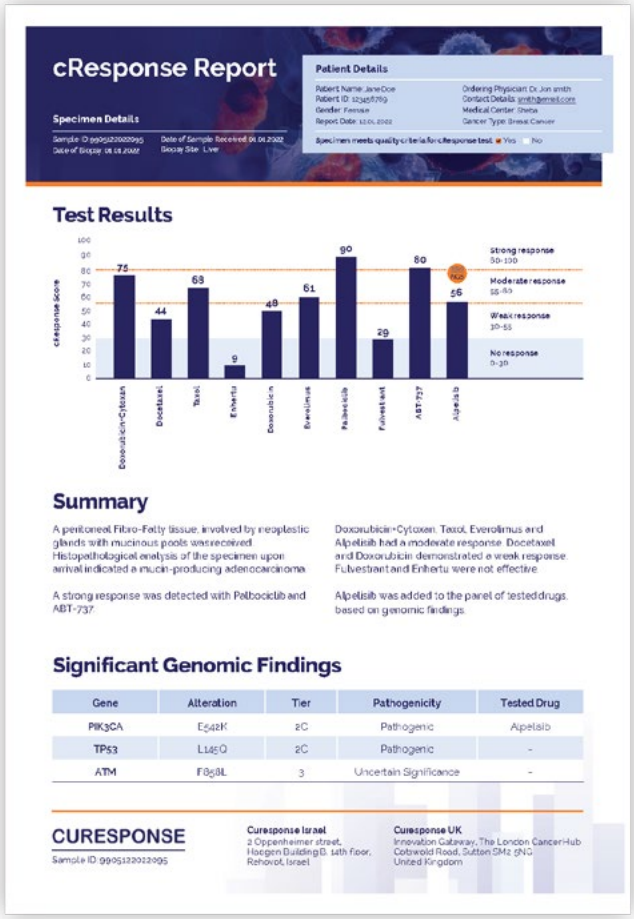
The gene panel includes 288 amplicons covering regions of therapeutic significance in 58 genes

ABL1, AKT1, ALK, APC, ATM, BRAF, CDH1, CDKN2A, CSF1R, CTNNB1, DDR2, DNMT3A, EGFR, ERBB2, ERBB4, ESR1, EZH2, FBXW7, FGFR1, FGFR2, FGFR3, FLT3, FOXL2, GNA11, GNAQ, GNAS, HNF1A, HRAS, IDH1, IDH2, JAK2, JAK3, KDR, KIT, KRAS, MAP2K1, MET, MLH1, MPL, MSH6, NOTCH1, NMP1, NRAS, PDGFRA, PIK3CA, PTEN, PTPN11, RB1, RET, SMAD4, SMARCB1, SMO, SRC, STK11, TP53 (full CDS coverage), TSC1, TSC2, VHL.

Test report

At the end of the testing and analysis process, a detailed report will be issued summarizing the degree of sensitivity of the patient's specific tumor to the drugs and the various drug combinations tested on the cResponse™ platform, as well as the genomic information received from the rapid sequencing test.

During the test, an algorithm developed by Curesponse is used which rates each drug or combination of drugs in a weighted score from 0 to 100, where 100 indicates a strong response to the treatment, that is, destruction of the tumor by the drug, and 0 indicates no response. The treatments with the highest weighted score reflect those treatments to which the tumor tissue was particularly sensitive and responded most strongly to on the test platform, and which should result in a more significant clinical response.



cResponse Report

Patient Details

Specimen Details

Test Results

Summary

A peritoneal Fibro-Fatty tissue, involved by neoplastic glands with mucinous pools was received. Histopathological analysis of the specimen upon arrival indicated a mucin-producing adenocarcinoma.

A strong response was detected with Palbociclib and ABT-737.

Doxorubicin+Cytoxen, Taxol, Everolimus and Alpelisib had a moderate response. Docetaxel and Doxorubicin demonstrated a weak response. Fulvestrant and Enhertu were not effective.

Alpelisib was added to the panel of tested drugs based on genomic findings.

Significant Genomic Findings

Gene	Alteration	Tier	Pathogenicity	Tested Drug
PIK3CA	E542K	2C	Pathogenic	Alpelisib
TP53	L145Q	2C	Pathogenic	-
ATM	F858L	3	Uncertain Significance	-

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Curesponse Israel

Curesponse UK

The process of making therapeutic decisions in cancer patients

Each treatment can be a single drug or a combination of drugs

A standard treatment	A treatment based on cResponse™ test

A B C D

Treatment C receives the highest score in the cResponse test and is selected by the oncologist

1 A

If treatment A fails

2 B

If treatment B fails

3 C

If treatment C fails

Treatment options are limited

1 C

If the patient develops resistance to treatment C, the oncologist will recommend treatment D, which received the second highest score in the test

2 D

If the patient develops resistance to treatment D

Additional treatment options tested in the cResponse test

cResponse™

- **A combination of rapid genomic sequencing and assessment of tumor sensitivity to various anticancer drugs for finding the optimal treatment.**
- **Assists in prioritizing cancer treatments according to their effectiveness for each patient.**
- **Testing sensitivity to chemotherapy and innovative biological treatments, both as a single drug and as a combination of several drugs.**
- **Avoidance of ineffective treatments and unnecessary side effects.**
- **Quick results within 14 business days.**
- **Financial coverage in Israel by some of the health funds and most health insurance companies (according to policy conditions).**
- **Personalized treatment for cancer patients.**

Disclaimer:

Please note the cResponse™ test is intended for use by licensed medical professionals for the purpose of information only. The report does not constitute a clinical diagnostic report, medical consultation or diagnosis, and does not constitute a substitute for professional consultation of a licensed health entity. In addition, the report is not intended for use as a sole source of input for diagnosis, prognosis, or as the main basis for reaching a treatment decision, and the medical history should always be considered during any treatment decision making and on determining the best choice of treatment based on the experience and the clinical judgement of the treating physician. Any treatment decision remains the full responsibility of the treating medical entity.

Curesponse does not take responsibility and does not promise the efficacy of any specific procedure, specific resources, specific tests, physician or other specific heath service providers, specific drugs, specific biological preparations, specific medical instruments or other specific products, specific procedures, specific opinions, or other specific information which may be noted in the report.

Curesponse does not promise and does not guarantee that any drug mentioned in the report will be efficient for treatment of the disease in any patient or does not promise or guarantee the effects that the drugs might have on the patient.

The cResponse™ test is carried out on fresh tissue received at the Curesponse laboratories within forty-eight (48) hours. Tissue samples are received and transferred under specific conditions, as required for analysis and reporting. Curesponse is responsible for coordination of tissue collection and delivery to Curesponse laboratories. The responsibility of tissue delivery is on the delivery company only.

Due to the Corona epidemic (Covid-19), there may be a delay in the delivery of certain tissue samples and as a result, the tissue quality may be badly influenced, which may make it difficult to perform the cResponse™ test and may affect the report received.

Curesponse makes great efforts in working with the delivery company in order to ensure that the tissue will arrive without unnecessary delay; however, Curesponse is not responsible for any delays.

CURESPONSE

Innovation Gateway, The London Cancer Hub,
Cotswold Road, Sutton, SM2 5NG, UK

+44 (0)20 8079 1278

Oppenheimer 2, Ha'Ogen Building B,
Rehovot, Israel

+972-74-7646101 +972-54-8991150

support@curesponse.tech