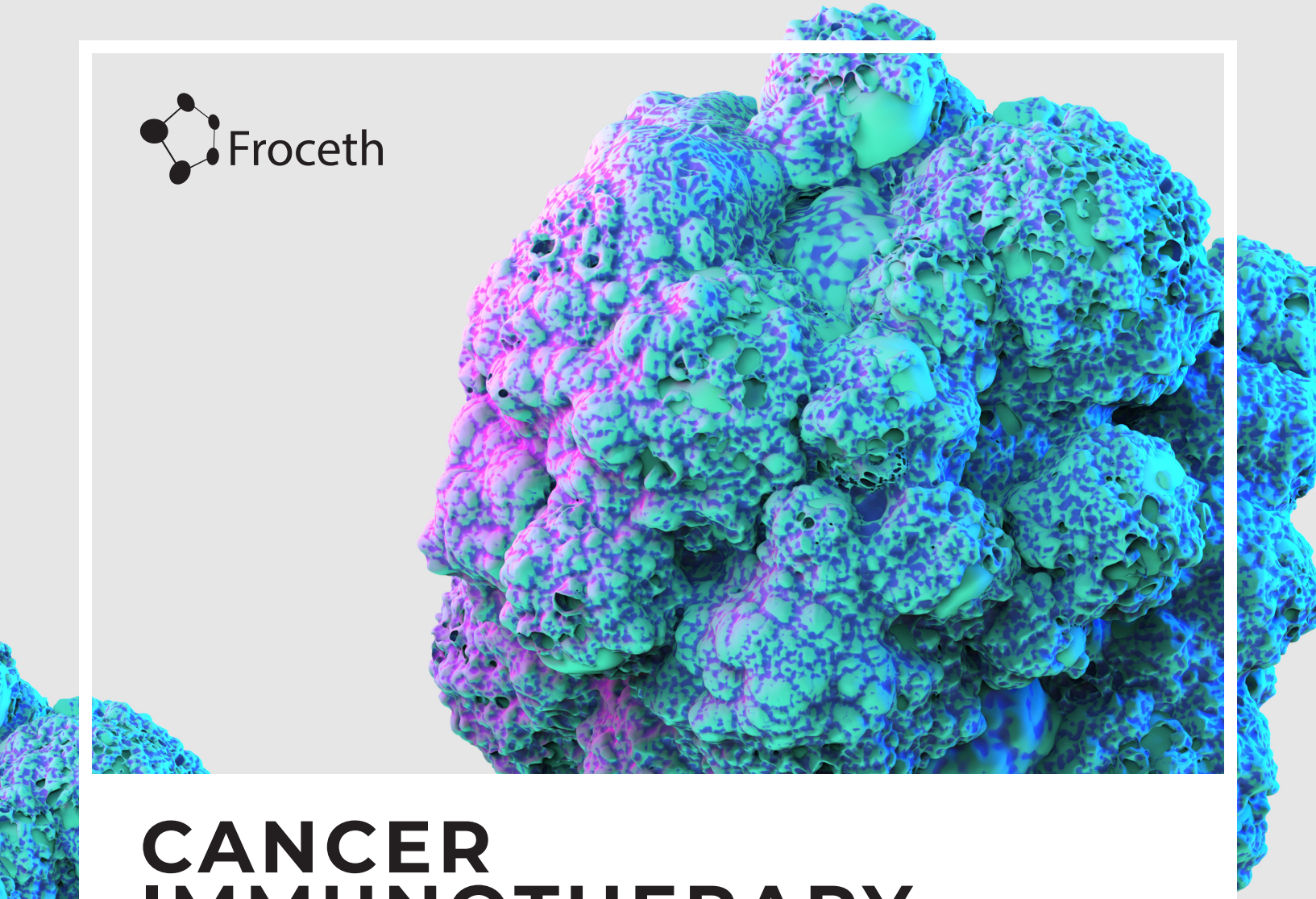
Froceth



CANCER IMMUNOTHERAPY

DENDRITIC CELL VACCINE & CYTOKINE INDUCED KILLERS

JSC Froceth
Mokslininku str. 6A,
08412 Vilnius, Lithuania

Contacts
info@froceth.lt
+370 648 37 591

Web
www.froceth.lt

Social
/frocethlt
/company/jsc-froceth

INTERACTION BETWEEN CANCER AND THE IMMUNE SYSTEM

ERADICATION

The immune system is unquestionably related to cancer formation, development and progression. It is believed that cancer cells can emerge at any time during the lifetime, especially with ageing. However, the components of the antitumor immune response eliminate them without any harmful effects to the organism.

EQUILIBRIUM

Some cancer cells may possess immune resistance mechanisms that enable them to avoid of being noticed by human immune system. In such cases, malignant cells are not eliminated, however the immune system is still capable of keeping them under control to prevent the formation of a detectable tumor. In such case, a dynamic balance settles between the tumour cells and the components of the immune system. The malignant cells are not completely destroyed, but remain under strict control of immune system, which suppress the development of clinically relevant tumours. Such state of balance between tumour cells and the immune system can last over decades or even a life-time without any signs of malignant disease.

EVASION

However, if the tumor cells tend to be more malignant and aggressive, the immune system may not be capable to destroy them completely. During the equilibrium phase, some tumor cells can acquire more potent and sophisticated molecular and cellular mechanisms enabling them to avoid the control of the immune system. At this phase of immune evasion cancer cells form a tumor, which can already be detected by diagnostic procedures and eventually becomes evident clinically.

TUMOR IMMUNOTHERAPY – HELPING THE IMMUNE SYSTEM TO FIGHT CANCER.

In recent years, immunotherapy has become an essential component of cancer treatment besides current standard therapies. In order to restore the ability of the immune system to control cancer, it is necessary to modulate its activity by applying tumor immunotherapy. There are many immunotherapeutic approaches and therapeutic cancer vaccination is one of the most promising among them. By applying cancer vaccination, it is sought to ensure the long term anti-tumour immune response, which protects the organism from cancer renewal (relapse) of its progression (metastases and spread in the body). Furthermore, therapeutic cancer vaccination is expected to induce long-lasting memory immune responses, which have to prevent a relapse or progression of cancer or increase the sensitivity of the tumor cells to subsequent standard cancer treatment methods, such as radiotherapy, chemotherapy, hormone therapy, etc.

IMMUNOTHERAPY WITH DENDRITIC CELL VACCINES (DCV)

Specific active immunotherapy with Dendritic Cell Vaccines (DCV) is a newly emerging and potent form of cancer immunotherapy that has clinically relevant mechanisms of action with great potential for the systemic treatment of cancers. It aims to reprogram the anti-tumour immune response from cancer accepting (tolerogenic) to cancer destroying (immunogenic) state. DCV does not affect the cancer directly; the therapeutic effect is instead caused by “nurturing” the immune system so that rather than tolerating the cancer cells, it recognizes them and takes action to control their activities.

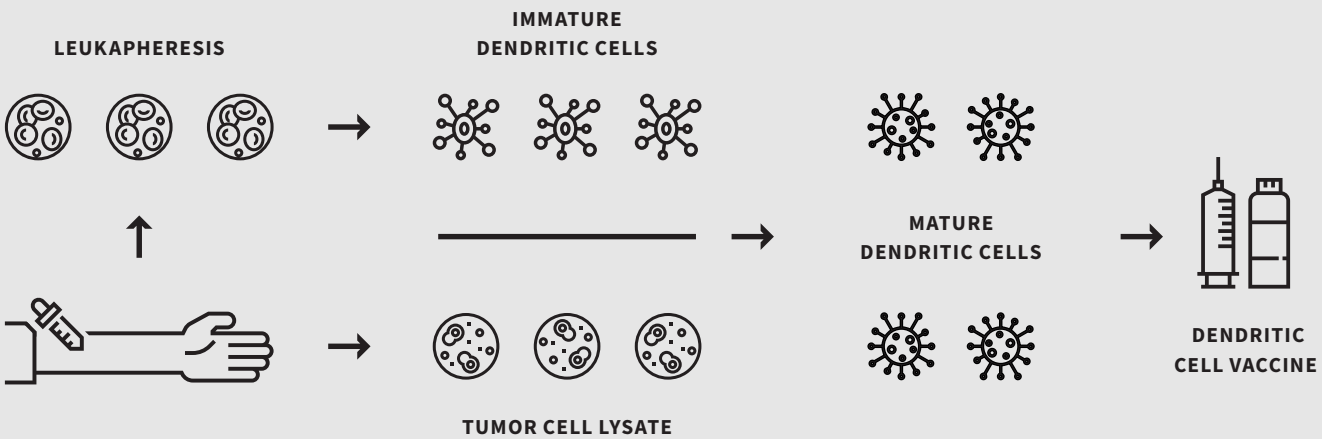
The active ingredients in this vaccine are dendritic cells designed to activate the patient’s immune system to restore their body’s ability to control the activities of cancer cells. Immunotherapy with dendritic cell vaccine (DCV) is a personalized cancer therapy, whose applicability to a particular patient is determined by various factors, including patient’s general health status and comorbidities, cancer stage as well as standard treatment strategy.

MANUFACTURING PROCESS

Dendritic cells are collected from patient’s blood, loaded with tumor antigens and matured in a specially designed GMP (Good Manufacturing Practice) laboratory which meets strict quality control and surveillance requirements. Once loaded with tumour antigens and matured correctly, dendritic cells are being activated to induce the immune response when injected back into patient’s bloodstream. DCV are manufactured within 4 weeks from the day of blood collection.

Since 2018, JSC Froceth has the permission to produce not only an Autologous but also an Allogenic dendritic cell vaccine which are eligible for any type of solid tumor including melanoma, breast, ovarian, lung, cervical, prostate, colorectal, brain cancer, etc. The blood for vaccine production may be taken not only from a patient itself, but also from his first-degree relative (from parent or child). In this case allogenic dendritic cell vaccine is produced. This method is especially useful in cases when the patient cannot donate the blood, for example, after chemotherapy when he encounters low blood count.

AUTOLOGOUS DENDRITIC CELL VACCINE MANUFACTURING



CLINICAL EFFECTIVENESS

The clinical response to therapeutic cancer vaccines is observed in about 55% of patients suffering from advanced (stage III-IV) cancer. However, the effectiveness may be even higher if:

Immunotherapy is combined with chemotherapy, hormone therapy or other forms of immunotherapy.

-

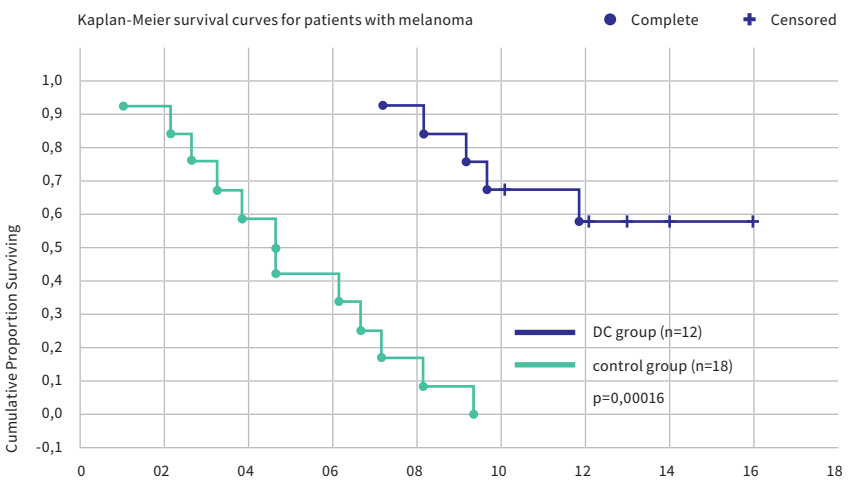
Immunotherapy is applied during the earlier stages of cancer.

-

We evaluated the efficacy of dendritic cell vaccines for cancer patients. Study consisted of 24 patients with terminal-stage metastatic cutaneous melanoma, 36 patients with terminal stage ovarian cancer, 40 patients with recurrent glioblastoma multiforme.

12 melanoma and 18 ovarian cancer patients were treated with autologous, monocyte-derived, tumor-lysate loaded, mature Dendritic cells (DC group), while 12 (melanoma) and 18 (ovarian cancer) clinically-matched patients received standard care (control group).

20 glioblastoma multiforme patients received standard treatment combined with therapeutic DC vaccination (st+DC group), while 20 clinically-matched patients respectively received standard care (control group). Patients in both groups were matched by age and clinical parameters.



A // MELANOMA

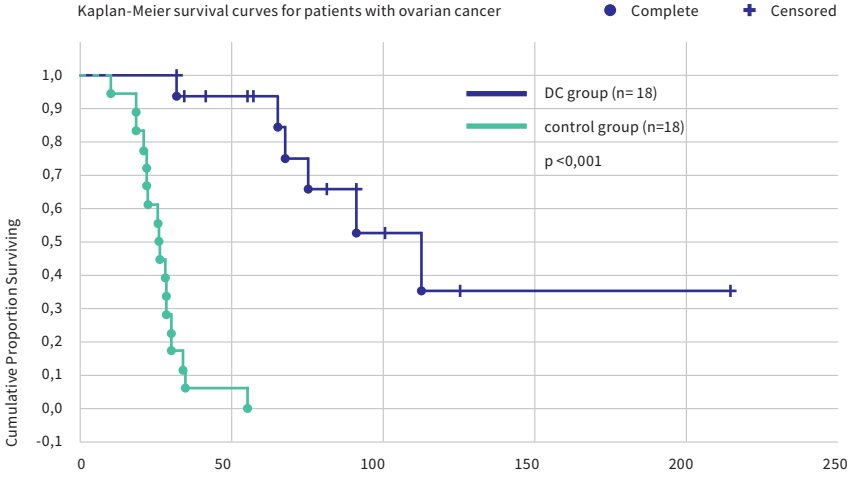
-

OVERALL SURVIVAL RATES

6-MONTH OS RATE:
100% in DC group vs 41.6% in control group

12-MONTH OS RATE:
58.3% in DC group vs 0% in control group

Time (months)



B // OVARIAN CANCER

-

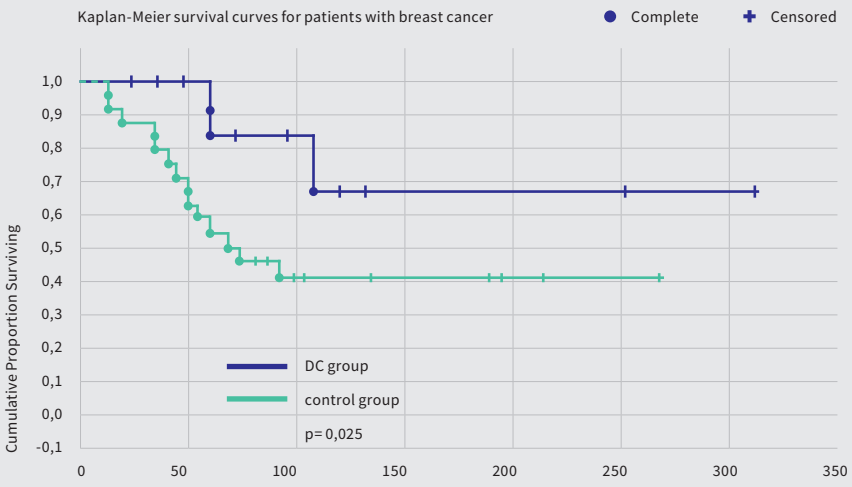
OVERALL SURVIVAL RATES

12-MONTH OS RATE:
100% in DC group vs 94.4% in control group

24-MONTH OS RATE:
100% in DC group vs 61.1% in control group

36-MONTH OS RATE:
94.4% in DC group vs 5.5% in control group

Time (months)

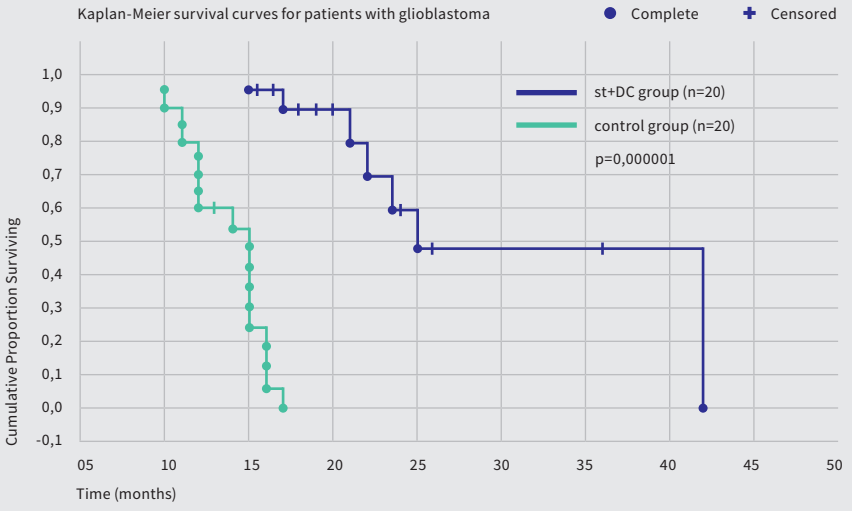


C //
BREAST CANCER

-

MEDIAN OVERALL SURVIVAL RATES

24 MONTHS (DC group)
VS
13 MONTHS (control group)



D //
GLIOBLASTOMA

-

OVERALL SURVIVAL RATES

12-MONTH OS RATE:
100% in the st+DC group vs 80% in the control group.
18-MONTH OS RATE:
80% in the st+DC group vs 0% in the control group.
24-MONTH OS RATE:
30% in the st+DC group vs 0% in the control group.
36-MONTH OS RATE:
10% in the st+DC group vs 0% in the control group.

ACTIVE IMMUNOTHERAPY

In contrast to chemotherapy, most active immunotherapeutic agents like DCV do not have direct killing activity on cancer cells, but rather act indirectly by reprogramming the antitumor immune response from the state of immune tolerance to the state of immune-mediated control of cancer. This is a dynamic multi-stage process that aims at restoring and establishing immune competence of antitumor immunity. Therefore, it requires much more time to establish a meaningful disease control (complete or partial tumor shrinkage or durable stable disease). Thus, the onset of clinical effect of many immunotherapeutic approaches is often delayed and can take up to 6–9 months to become evident.

CYTOKINE INDUCED KILLERS (CIK)

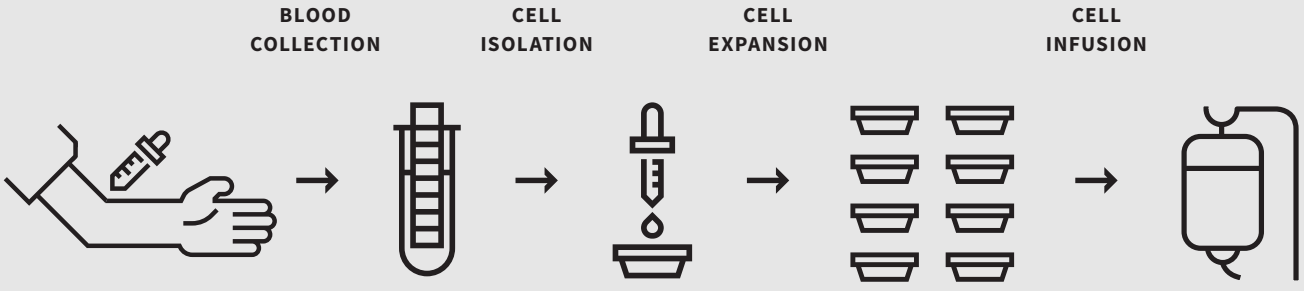
Cytokine-induced killer (CIK) cells are currently emerging as a promising and effective treatment option, especially when combined with standard therapy in an adjuvant treatment setting, but can successfully be used as a monotherapy as well. Unlike active immunotherapy with Dendritic cell vaccines, Cytokine induced killers (CIK) have a direct killing effect on tumor cells, which in general can be termed as passive immunotherapy. A large amount of clinical trials demonstrated encouraging results and showed that CIK cells may prevent recurrence, improve the progression as well as the overall survival while enhancing quality of life in cancer patients.

CIK cells are a mixture of T-lymphocytes, which are ex vivo expanded with cytokines, comprising CD3+/CD56+ cells, CD56+ natural killer (NK) cells, and CD3+ cytotoxic T cells. Among them, CD3+/CD56+ T cells, which are rare in uncultured peripheral blood, are the main effector cells. They have a high proliferation rate, potent antitumor effects with the dual-functional capability of both T cells and NK cells, and little cytotoxicity to normal cells, but with substantial specificity to tumor cells.

CIK cells are not restricted to tumour type or origin, therefore can be used for treatment of patients with any diagnosis, as long as it is done in autologous regime.

MANUFACTURING PROCESS

CIKs are expanded from the patient's peripheral blood mononuclear cells and are able to proliferate rapidly with the timed addition of cytokines, such as interleukin 2, interferon γ and anti CD3 monoclonal antibody in vitro. All CIK cell cultures are tested for contamination (bacteria, fungi, and mycoplasma) throughout the manufacturing process to assure culture quality and transfusion safety. CIK are manufactured within 4 weeks from the day of blood collection.



Once reintroduced to the patients' body, CIKs home in onto the tumor site to kill cancer cells directly. They are able to sense the tumor by danger signals sent by the patients' body. Their action is immediate, as they are applied in a fully developed state. They do not need any assistance from the patient's own immune system, which makes this therapy available to patients whose immune system is too weak to contribute to an effective immune response. This puts CIKs in the category of passive immunotherapy, as they substitute for patients' immune system, rather than utilize it.

COMBINATIONAL THERAPY – A KEY TO SUCCESS

It was shown that active participation of the immune system in the destruction of malignant cells is essential for the therapeutic activity of chemotherapy, radiation therapy as well as hormone therapy and many targeted therapies. There is data that chemotherapy and radiotherapy increase cancer response to immunotherapy and vice versa. Thus, it is very likely that even if the diseases relapses during or after the immunotherapeutic treatment, a beneficial effect of immunotherapy still remains because it is supposed to increase tumor response to the next-line treatment, mostly chemotherapy. Based on this data, the concept of chemoimmunotherapy is proposed and it states that a reasonable combination of immunotherapy with other cancer treatment approaches is pivotal in order to achieve a meaningful and long-lasting cancer control.

Passive immunotherapy, like CIKs or monoclonal antibody therapies, combine well with Active immunotherapy like DCV, which mobilizes patients' immune system. Such a combination has the benefits of the immediate effect of the passive therapy arm and the long term effect developed in the course of active immunotherapy arm. Immunotherapies with both CIKs and DCVs are an advanced combination therapy as they work on very different principles, which contributes to a broad, complex immune response against cancer.

With two different cell-based products, JSC Froceth has a broad arsenal of immunotherapies, making us the definite leader in the Eastern Europe and equal partners in our contacts with Western medical professionals.

01 //

-

Immunotherapy with DCV and CIK is not yet a standard cancer treatment method, but can be used as an additive advanced therapy.

02 //

-

Immunotherapy with DCV and CIK can be used as an adjuvant or palliative treatment for various malignancies.

03 //

-

Immunotherapy with DCV and CIK is a personalized cancer therapy, whose applicability to a particular patient is determined by various factors, including:

- patient's general health status and comorbidities;
- cancer stage;
- standard treatment strategy (previous or ongoing anticancer therapies and disease response to them).

04 //

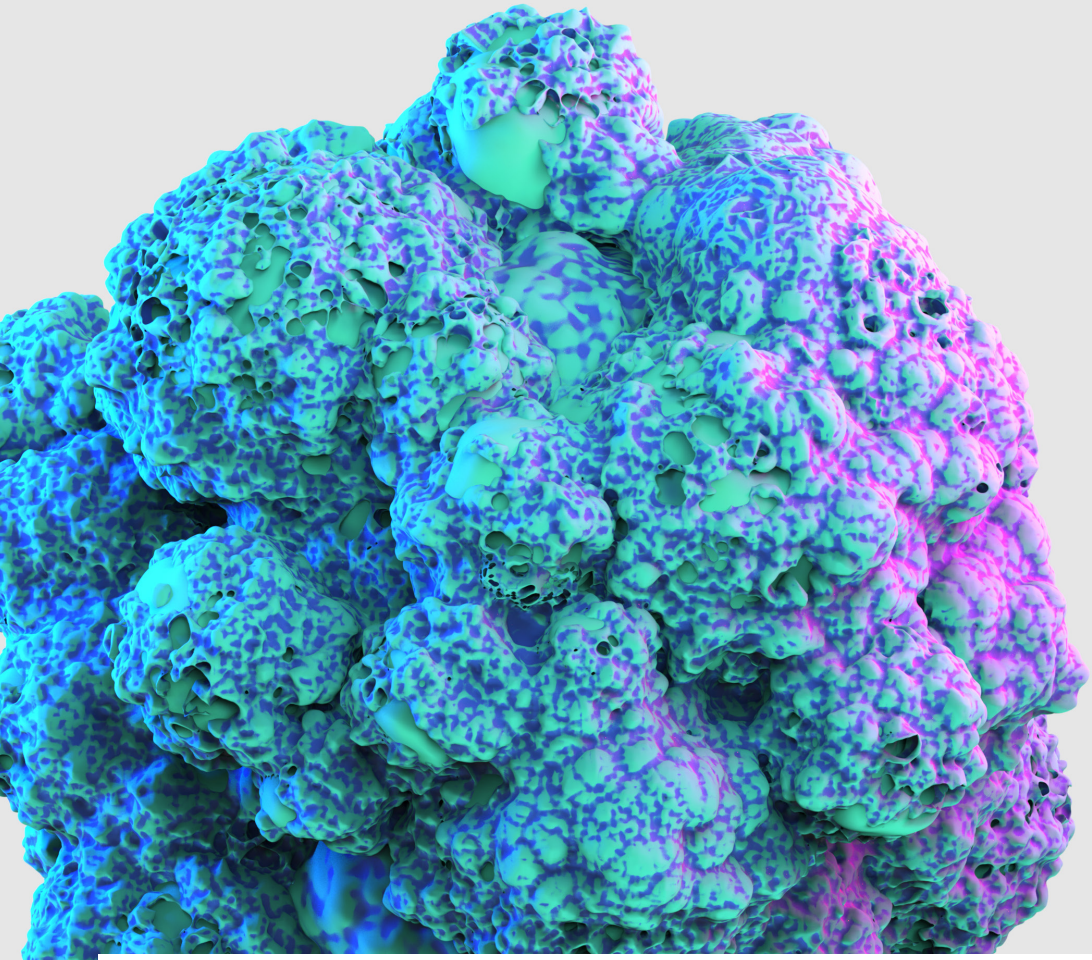
-

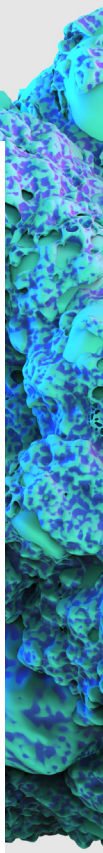
Immunotherapy with DCV and CIK can be combined with chemotherapy, hormone therapy, targeted therapies, radiotherapy or other immunotherapeutic methods.

05 //

-

Immunotherapy with DCV and CIK are applied by multidisciplinary team of oncologists and immunologists, together with standard treatment or after its completion.





CONTACT US

JSC Froceth
Moksliininku str. 6A,
08412 Vilnius, Lithuania

Contacts
info@froceth.lt
+370 648 37 591

Web
www.froceth.lt

Social
/frocethlt
/company/jsc-froceth