

ONCOLYTIC VIRUS FOR CANCER TREATMENT: THE REAL DIAMOND OF LATVIA

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The world's fight with cancer seems the never-ending story. The worst illness that every year takes away our beloved ones, leaves no family without loss, no soul without grief. Latvia is the lucky place where the idea about the virus to treat cancer was born, thanks to viruses' natural properties – proactively finding and killing the cancer cells, thus promising the mankind a cure of this deadly disease.

The first-ever registered oncolytic virus in the world – Rigvir (ECHO-7 virus strain) comes from the hands of honourable scientist Aina Muceniece who is the founder of practical virotherapy. The sequel, now described in just a few words, was the result of titanic

work, perseverance and desire to the science, and true willingness to help people. The virus itself became a safe one with high efficacy and well tolerated by patients, and even without significant side effects. It started in the 1960s, in Augusts Kirhenšteins Institute of Microbiology and Virology, where in a special laboratory the very first preclinical trials with animals were made, followed by safety and efficacy trials. Soon after that, clinical trials started in Rīga, Moscow, and Saratov. It became known that the oncolytic virus induces tumour cell lysis, local immunological reaction, and enhance systemic anti-tumour immunity.

At the same time, the science in the world, outside the Iron Curtain, took another direction. Nobody was speaking about oncolytic virotherapy in cancer treatment except Aina Muceniece, who was from the Soviet Union, in the hard embrace of KGB, which meant silence for the rest of the world.

The late 1980s came with a collapse of the previous regime, which brought freedom to Latvia, but fully stopped the pan-Soviet registration process of Rigvir, which was started before. Only a few years after 1991, when the restoration of the independence in Latvia was established, Rigvir was available for patients only experimentally. While the state was reborn, there were almost ten years of silence around this promising medication. Rigvir became a kind of a victim of an epoch, almost falling through the separator of the era. However, at the beginning of the new century, the scientists, who previously were working together with Aina Muceniece, came together once more for



Aina Muceniece with colleagues at the Institute of Microbiology and Virology (first row, fourth from left)

establishing the non-governmental organisation, with the one and only purpose – to restart Rigvir. The work went great and after a few years of decent work with all the materials, studies, and trial results collected and analysed, the revival of this medicine took place, followed by national registration in 2004. By 2005, Rigvir was already included in the TOP 10 of National Achievements, recognised by the Latvian Academy of Sciences, which was chaired by academician Jānis Stradiņš at that time.

On 14 February 2010, sad news were brought to the world about Aina Muceniece's demise. Her life had been filled with happiness, achievements, miraculous discoveries, inventing and entering into the circulation of Rigvir, and helping to save lives and life quality to thousands of cancer patients all around the globe, the motto of her life was "science, science unite, promise to protect mankind". This goes on thanks to her children and grandchildren, and colleagues who continue her work.

From 2011, when Rigvir medicine was included in the medicines reimbursement system of the state, it was applied for 65–70% of melanoma patients in Latvia. Collection and analysis of patient data in this

country showed amazing efficacy, revealing that using Rigvir for patients may prolong progression-free time and reduce mortality 4–6 times (publication in the journal *Melanoma Research*, 2015), which made many take a more serious look at oncolytic virotherapy as a perspective cancer treatment, and also at Rigvir. Further, the Horizont2020 grant was received, and the decent work with European Medicines Agency (EMA) resulted in EMA's scientific advice (at 2017), which stated: the available data are sufficient to enter any clinical trial phase II necessary for the central registration procedure in the future. In the meantime, Rigvir developers received several Seal of Excellence certificates from the European Commission and the prize WIPO for the high-level intellectual property patent protection.

The medicine under the name of Rigvir was registered as a drug for melanoma treatment in several countries – besides Latvia also in Georgia, Armenia, Uzbekistan.

Nowadays, real help for cancer patients is provided, using health tourism, in collaboration with the International Virotherapy Center. The scientists and healthcare organisers are participating in different



Contract signing ceremony during China International Import Expo, November 2019

medical and healthcare conferences all around the world reporting on the development of virotherapy. In 2018, deciding to restructure into a biotech company, Rigvir developers Rigvir Group purposefully decreased the volumes of commercialisation. This made it possible to attract the much-needed investment for further product development and research and, consequently, for subsequent registration of Rigvir in more developed markets or the sale of licenses. The successful development of previous years allowed attracting more investments within a short time, including from a venture fund and an international biotech company.

Year 2019 came with a new success – good laboratory practice (GLP) Toxicity Study was held, granted by the EU fund European Regional Development Fund, with the total cost of 560 000 EUR, which was completed in 2020 with the best possible result: no observed adverse effects (NOAEL). The study has just been published in the scientific journal *Toxicology Reports*.

In 2019, also, the first out-licensing deal in the Chinese market took place – the signing of the agreement was organised by the Chinese side as part of China International Import Expo in the presence of several thousand spectators.

Year 2020 ended with the completion of the final phase of the brand new laboratory and obtaining its

good manufacturing practice (GMP) certificate, with 2.3 million EUR invested in this project.

Today Rigvir Group has taken a convincing course to attract investments, which would allow continuation of research and successful implementation of a strategic direction in the markets of highly developed countries.

It should be noted that numerous publications have been issued since the beginning of Rigvir journey – both retrospective data, several unique case reports, and detailed descriptions of the appearance of Rigvir. Also, it is worth mentioning that the foundation created by Aina Muceniece's relatives implemented the incredible project when eight cancer patients (even in the 3rd and 4th stages of illness) attempted Mont Blanc. The ascent was filmed and the movie "Another Taste of Life" showing their courage to overcome themselves was shown later.

Since then, scientists of the world have become introduced to and investigated oncolytic virotherapy; now it is widely known that oncolytic viruses as a medication can be applied both as monotherapy and as combinations to increase the effectiveness of other therapies.

Life is a journey. Aina Muceniece's life definitely was. Life became a journey for each who got on Rigvir, the almighty ECHO-7 virus. Let the journey continue!



The new Rigvir laboratory building in Riga, Atlasa Street