# PERSONALIZED CANCER TREATMENTS

## NO LONGER A DREAM WITH NEW MEDICAL TECH

ADVA X3 IS A DEVICE THAT CAN CREATE LIFE-SAVING DRUGS AUTOMATICALLY AND CUSTOMIZED FOR EACH INDIVIDUAL PATIENT

BY TALIA LEVIN

In the past, when biologists and other scientists were asked what their greatest dream was, almost all of them would reply that, without a doubt, their greatest ambition was to find a cure for cancer. Now, at a time that many researchers are currently working diligently on COVID-19 issues, it might surprise some people to know that there already is a cure – or at least a partial cure – for some types of cancer.

CAR-T (aka Chimeric Antigen Receptor) cells are T cells that have been genetically engineered to produce an artificial T-cell receptor for use in immunotherapy. This breakthrough came three years ago, following more than 20 years of research.

Here is how it works. White blood cells harvested from a person are activated, expanded and genetically engineered. Afterward, these resulting CAR-T cells are re-infused into the patient so they can attack and destroy tumors. This method for curing cancer is already being used to combat certain types of leukemia, has received FDA approval and has been added to Israel's healthcare basket. In addition, hundreds of clinical trials are currently being carried out for other cancers and autoimmune diseases.

This is undoubtedly the beginning of a revolution. For the time being, however, these treatments will be available only to a tiny group of terminally ill cancer patients for whom no other treatment has been beneficial.

Fewer than 2,000 patients have been treated using this innovative method over the last three years. The reason is a combination of cost, logistics, lack of technology and conservative outlook.

"To date, this drug has only been manufactured manually in large clean rooms in the US or Europe, and not in hospitals," explains biologist Dr. Ohad Karnieli, the founder and CEO of ADVA Biotechnology, which developed the ADVA X3, a device that can create these same life-saving drugs automatically and customized for each individual. The ADVA X3 can do this efficiently, while also dramatically reducing manufacturing costs, which would make these treatments accessible to a much larger number of patients. As it stands today, even if a patient is entitled to this drug, he or she most likely will not receive it, since the process for producing it is complex and can take months. With ADVA X3, the drug can be produced on-site in a few weeks."

***Why has such a small amount of the drug been produced over the last three years?***

"First of all, the treatment costs $500,000 per patient. As a result, even though theoretically we have a practical solution for patients with leukemia and autoimmune diseases, there's almost no chance that they will actually receive the drug unless the patient is extremely wealthy and also very lucky. But it's not just a matter of money. Granted, Israel's healthcare basket allocated tens of millions of shekels for this drug last year, but this amount can only help a few dozen patients due to the complicated logistical issues."

Five years ago, Dr. Karnieli, who has a PhD in genetic engineering and stem cells, recognized that the CAR-T cell cure was an effective treatment. But in order to make the treatment accessible to as many patients as possible, he understood that a technological revolution must be initiated.

"On the one hand, my field is stem cell research, but I also have a technological background. It was crystal-clear to me that this was the winning combination."

Dr. Karnieli's solution is a printer-like machine that replaces the biological process of cell engineering, which up until now could only take place in a lab. You add the patient's blood in one side, and the contents that enable the cells to be genetically engineered to the other. The process takes seven to 10 days, at the end of which you have ready-made, customized engineered blood that can be re-infused into the patient. This device provides a customized, high-quality solution at a much lower cost than has been available up until now and with much greater accessibility.

According to Noam Bercovich, VP of development of ADVA Biotechnology, "The biggest advantage of the ADVA X3 is that it considerably lowers manufacturing costs, since you no longer have to send the blood overseas with a large team of biologists trained in this field so that they can engineer the blood and then bring it back. With the ADVA X3, you have a machine that sits on top of your table and any technician working in a hospital can operate it."

ADVA Biotechnology was created four years ago when Karnieli and his partners realized that the methodology that pharmaceutical companies were currently following was illogical and could not be adapted to modern personalized medicine.

"Imagine if we could put a few

of these machines in every hospital," continues Karnieli. "They could then be used to produce a specific customized drug for each cancer patient. This would be tantamount to a revolution, not only by making this treatment accessible to every single patient, but by changing the model according to which the industry functions."

***How would you characterize the pharmaceutical industry as it stands today?***

"Pharma companies carry out their manufacturing in large factories and charge thousands of dollars for each dose of this treatment. Once this drug can be manufactured in hospitals or at small local labs owned by pharmaceutical companies, this will make production and transport much more accessible than it is today."

Some of the challenges experienced thus far are no longer obstacles. The technology that will replace the manual method used in labs up until now already exists.

"The machine works and we have already completed quite a few runs, so this stage is now behind us," says Karnieli. "Now, we need to overcome the next challenge: marketing and sales. Our model enables all of the market players to improve access to this life-saving medicine. Hospitals and medical centers will be capable of producing the drug on their own, which will make treating patients so much simpler.

"In addition, this also provides pharma companies with an excellent solution. One option is that they can produce and distribute just the API [Active Pharmaceutical Ingredient], the component that enables genetic manipulation, and then the production can be carried out in hospitals. A second possibility is that pharma companies will build a number of centers in certain countries, which would still be simpler than how the drug is manufactured today in large clean rooms and then distributed worldwide. In this model, there'd be a decentralized distribution network that produces customized drugs in closer proximity to patients."

***Is there a demand in hospitals for this service?***

"Yes. A number of hospitals around the world are already using our device. At Sheba, for example, they've been using our device for a few years already. They are using the regular manual method, in the hope that soon they too will be able to use our machine to increase the hospital's ability to treat more patients. In practice today, many hospitals are producing a small amount of medicine since the large companies are failing to meet demand.

"Think about it this way: Pharma companies have invested millions of dollars to build factories that produce this drug, but in actuality they've only managed to produce less than 2,000 doses over the last three years. They are far from meeting demand. Even if people have the money to pay for the treatment, it's not always manufactured in time. This was the impetus behind our development of the ADVA X3, which makes this life-saving drug so much more accessible."

***How realistic is your model?***

"In our opinion, it's extremely realistic, since our machine will work well in the scenario in which production will take place inside hospitals, with the API being supplied by pharmaceutical companies, and also for the possibility that the pharma companies will carry out production in local centers [there will be one for all of Israel, for example]. Both of these scenarios will become much simpler

*(Courtesy)*

when used in conjunction with our machines.

"The ADVA X3 will simplify production and ensure that immune cell therapy will be more cost effective and speedier," explains Karnieli. "Instead of pharma companies having one massive factory with lots of employees who are carrying out the production of the drug manually, it will employ many of these devices, which will greatly speed up output. Imagine how much quicker it will be if we have a center here in Israel that could supply doses to all of our hospitals. This will solve the problem of long lead time and the complicated logistics of transporting materials overseas and then back to Israel."

***What kind of savings are we talking about?***

"Production in hospitals will cost one-quarter of the current price. They won't... take $300,000, but less. And we want to be able to produce much more than 2,000 doses over three years. Why should a cancer patient have to suffer through such a long battery of treatments and then still have to wait for his turn to perhaps receive a dose of this unique treatment when there's a way to overcome this obstacle? And once patients learn about this treatment that can save their life, why would they be willing to suffer through extensive and difficult treatments when they know there's very little chance of it being effective? Why not give patients the chance to receive the drug at an earlier stage in the disease? It's not just an issue of money. Only pressure from the public will influence the regulator to approve production."

***What type of personnel are needed for this type of production?***

"In hospitals, biologists are in charge of the production process. Doctors choose which patients are eligible for the treatment, and they instruct us regarding their goal so that we can understand how to engineer the cells exactly as needed for each individual patient."

It's pretty amazing to realize that in 2021 we have the capability not just to prolong cancer patients' lives, but to heal them. Now the challenge for ADVA Biotechnology, which develops and manufactures its products here in Israel, is to convince the world that the next big thing is enabling everyone who needs their drug to have access to it.

*(Photo by Freepik.com)*

"Two years ago, we were busy filling bottles and tubes. We lit our burners, began recruiting people to join our team, and then founded our company. Our clients around the world include pharmaceutical companies, hospitals and universities. We produced the treatment for them, proving that our machine is capable of producing the same exact drug in a much more efficient, cost-effective and simpler way. Over the next year, these institutions will receive one of our machines so they can begin experimenting with them. The next stage will hopefully be large-scale production."

***What's your vision?***

"To make these amazing life-saving treatments accessible to patients," says Ofra Toledo, VP of business development for ADVA Biotechnology. "To offer everyone the opportunity to receive the best treatment that has been personalized just for them. It's already happening. We are targeting both the Israeli and international markets. We have quite a few interested clients in Europe, the US and the Far East, and we are currently introducing our product into hospitals and medical centers here in Israel."

***What has the response been like?***

"Absolutely fantastic! We've had such great feedback from medical professionals, industry leaders and investors, too. Our biggest challenge is penetrating such a conservative market. Biologics are so much more complex than chemical drugs. They are live cells that need to be re-engineered so that they can attack an extremely specific cancer. Most scientists are conservative and are extremely cautious when it comes to this type of technology, since they are used to working a certain way.

"We totally get that lab work is not industrial, but what we can accomplish with our machine does not completely eliminate the need for lab work. We have a challenge before us. No hospital or company has told us our device is amazing, but that's okay because it takes time for people to get used to using new methods. We are planning to carry out a number of pilot programs here in Israel, as well as overseas, so that our clients can experience the success of our platform first-hand. Then we will start manufacturing on a larger scale."

*Translated by Hannah Hochner. This article was written in cooperation with Adva.*