Mrna Vaccines: The Next Frontier in the Fight Against Pancreatic Cancer"- A Review Article

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***Abstract*—Pancreatic cancer is one of the deadliest malignancies in human beings across the globe, with its treatment accompanied by poor prognosis due to its diagnosis at late stages and resistance to the common cancer treatments, i.e. chemo and radiation.[1] The existing regimens have relatively low effectiveness and are burdened by a great deal of systemic toxicity, which further reinforces the need to develop individually crafted treatment strategies. These gaps will be occupied by new strategies like the mRNA-based cancer vaccines that are anticipated to cause minimal to no side effects and induce tumor-restricted immune responses. Very early Phase-I trials have shown that about half of the pancreatic cancer patients who are given personalized mRNA vaccines develop strong anti-tumor immune responses, pointing to the potential of this new intervention as a potentially effective, personalized therapy for pancreatic cancer that is much more aggressive and has a poor prognosis.[2]**

1. INTRODUCTION

Pancreatic cancer belongs to the group of the most aggressive and lethal types of cancer and occupies a top-ranking position as the 7th global human cause of cancer deaths. It gets diagnosed and at highly advanced stages because it has no early symptoms and no sure screening procedures. The likely signs, e.g. jaundice, unexplained weight loss, abdominal pain, and digestive disruptions, only display themselves in the advanced stages, making its prognosis low. The pancreatic tumors have dense stroma, massive evasion, and metastasize rapidly at the cellular level. The most common histological variant is pancreatic ductal adenocarcinoma (PDAC), that is highly resistant to apoptosis and medical therapy. The present treatment modalities, such as surgery, chemotherapy and radiotherapy, have limited survival advantage and tend to be severely toxic. Even the targeted therapies have limited gains in the long-term outcome.

CT, MRI, etc are mostly utilized in the diagnosis and endoscopic biopsy, as well as tumor markers such as CA 19-9, contributes to this. Nevertheless, they are not able to identify tumors most of the time at an easily curable stage. The main aspect in the prevention is still lifestyle changes, including moderation of smoking, obesity, and alcoholism. Due to these difficulties, there is an immediate need to move away from a more individualized treatment towards one size fits all regimens. It has paved the way for new modes of interventions in the form of RNA-based immunotherapy, particularly mRNA vaccines, which are promising in the specificity, reduced toxicity, and narrower probable target, as is the case with the activation of the immune system against the tumor cells.[3]

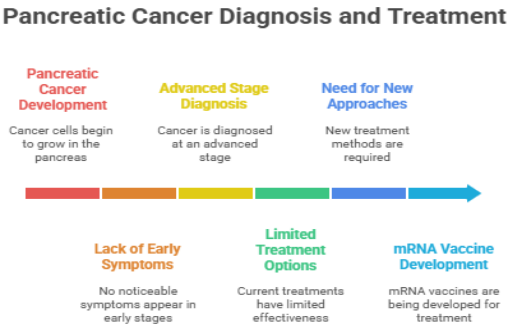

Fig.1 Pancreatic Cancer Diagnosis and Treatment. Created by the author based on data from [3]

2. NOVEL SOLUTIONS FOR TREATING PANCREATIC CANCER: MRNA VACCINES

The topic of mRNA vaccine use in the treatment of oncological disease is becoming increasingly important, especially when it comes to the treatment of highly lethal neoplasia. Pancreatic cancer, with its five-year survival rate of approximately 13%, is one example that highlights this

category which presents difficult therapeutic options. Early identification is still rare, and the disease often advances even with combination therapies, which in most cases entail surgical resection, chemotherapy, and radiation. One issue is that resistance to these targeted therapeutic and immunotherapeutic agents is quickly becoming an issue and adding to the problem.

The resistance of pancreatic cancer to radiation, and the hurdle in finding an effective screening method, is a major obstacle to a satisfactory therapy. Under such a clinical setting, mRNA-based vaccines will offer an opportunity to conduct personalized immunotherapy, where there is a focus to target immune-effectors against tumor-specific antigens. The review is therefore examining the potential in which mRNA vaccines have opened up the world where pancreatic cancer may be treated differently.[4]

3. WHAT ARE MRNA CANCER VACCINES?

Cancer immunotherapy through mRNA cancer vaccines uses the in-vitro transmission of synthetic messenger RNA to target cells of the host to induce production of tumor-specific proteins, all of which are generically called neoantigens. The adaptive immune response to these proteins, which does not occur in normal tissues but can be considered as non-self, triggers a specific antitumor response. Unlike prophylactic vaccines, mRNA vaccines are therapeutic: they are used to control existing cancer by teaching the immune system which cells to destroy; accordingly, they target the presence of cognate neoantigens on cancer cells.[5]

4. THE MECHANISM OF ACTION

These mRNA-based vaccines take advantage of the protein production machinery kept by the host in order to mount tumor-specific adaptive immunity against the tumor. When injected intramuscularly, mRNA in lipid nanoparticles is absorbed by dendritic cells, which are also the key players in antigen presentation. The mRNA is translated in the dendritic cell to create neoantigens, which are new proteins found as the result of somatic mutations exclusive to the tumor. The exposure of these neoantigens on the surface of cells subsequently exposes them to cytotoxic T-cells which expand, and consequently, these characteristics are recognized as tumors.

Victims of cancer immunotherapy have impairments due to the challenge of determining tumor and normal self. Despite this, pancreatic tumors of long-term survivors appear to have an extraordinarily high burden of neoantigens, which makes the disease more immunogenic than it should be, and the mRNA vaccine is an optimal candidate, as it would allow encoding and presentation of patient-specific neoantigens, thus maintaining high T-cell immunity.[6]

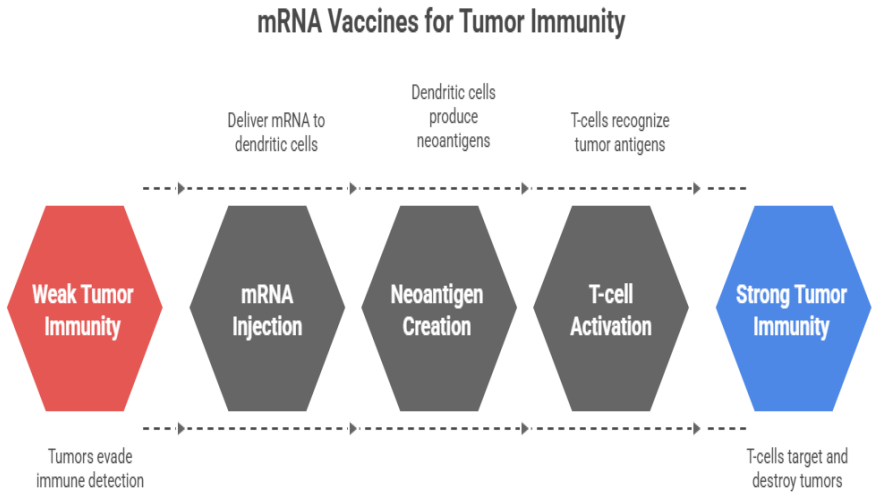

Fig.2 Mechanism of action of mRNA vaccines. Created by the author based on data from [6]

5. CASE STUDY: DR. VINOD BALACHANDRAN AND AUTOGENE CEVUMERAN

The Autogene Cevumeran is a personalized mRNA vaccine that was developed at Memorial Sloan Kettering Cancer Center and whose concept was developed by physician-scientist Dr. Vinod Balachandran. The clinical trial consisted of the Phase I trial with 16 patients of personalized vaccination according to the mutation profile of the tumor and, therefore, caused a particular response in the patient. As demonstrated and reported in Nature (2023), the vaccine was shown to be safe, and it was found that 50% of participants experienced T-cell activation. In patients who developed an immune response, the incidence of cancer recurrence was significantly decreased 1.5 years after follow-up. The durability of vaccine-induced T cells was demonstrated to be over four years even in patients undergoing chemotherapy, which was confirmed an independent analysis in 2025, confirming that it was durable and therapeutically compatible.

The responders had been observed at the end of three years; six of the eight responders had been cancer-free, but the other two with less vigorous immune reactions had recurrence. These findings bode well in terms of the future of mRNA-based vaccination to induce extended antitumor immunity, a positive change that can lead to progress when compared to current methods. Therefore, Autogene Cevumeran can be regarded as one of the most striking examples of how mRNA vaccines can transform the care of pancreatic cancer. Vaccines in the Phase I trial were custom-made using the profile of the tumor of the patient. Following surgical excision of the tumor, the DNA that was sequenced showed around 20 mutations that were assumed to produce neoantigens that would likely produce an immune response most probably to occur. BioNTech produced the respective mRNA and used the vaccine as a multi-dose regimen to maintain immunological stimulation.[7]

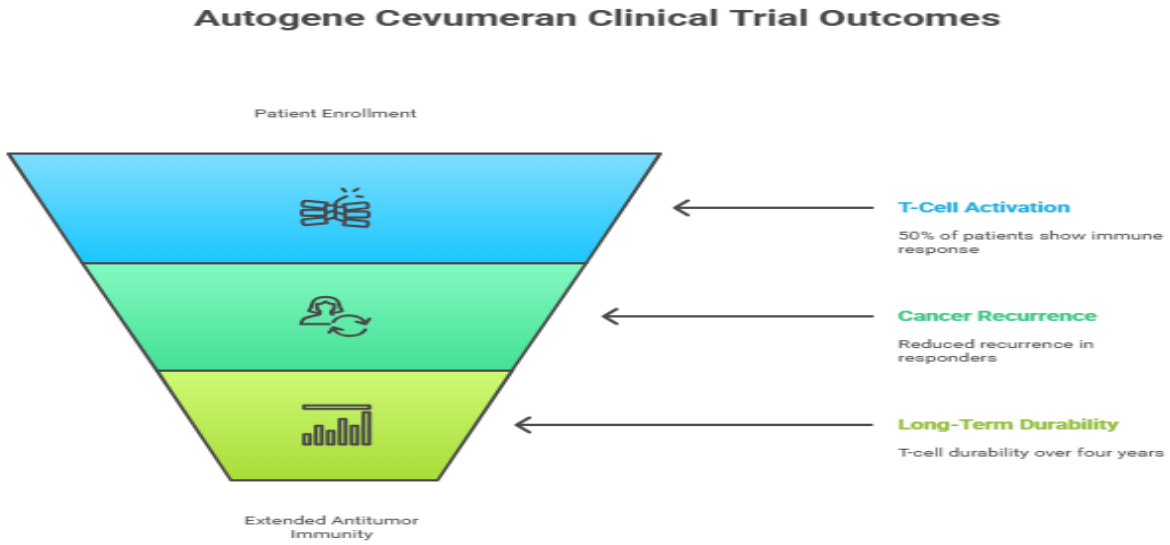

Fig.3 Clinical trial outcomes of the mRNA vaccine Autogene Cevumeran in pancreatic cancer. Created by the author based on data from [7]

6. ADVANTAGES OF MRNA VACCINES OVER TRADITIONAL TREATMENTS

Unlike traditional therapeutic approaches like chemotherapy and radiation, mRNA vaccines have a well-targeted and very intricate approach. These agents stimulate the development of tumor-specific immunological responses that have high specificity to the tumors they encode, and hence off-target effects are minimal, and the correlated side effects are small. The existing methods of pancreatic cancer treatment can hardly provide long-lasting immunological safety; on the contrary, mRNA vaccines encourage strong immune memory formation and can help avoid the recurrence of the disease. Autogene Cevumeran mRNA vaccine was very safe and well tolerated, and no serious adverse event was identified. Notably, the vaccine may be used alongside the current treatment regimens; in the Phase I trial, the patients were also given atezolizumab (a checkpoint inhibitor) to increase the efficacy of the immune response, which shows therapeutic compatibility and synergistic effect.[8]

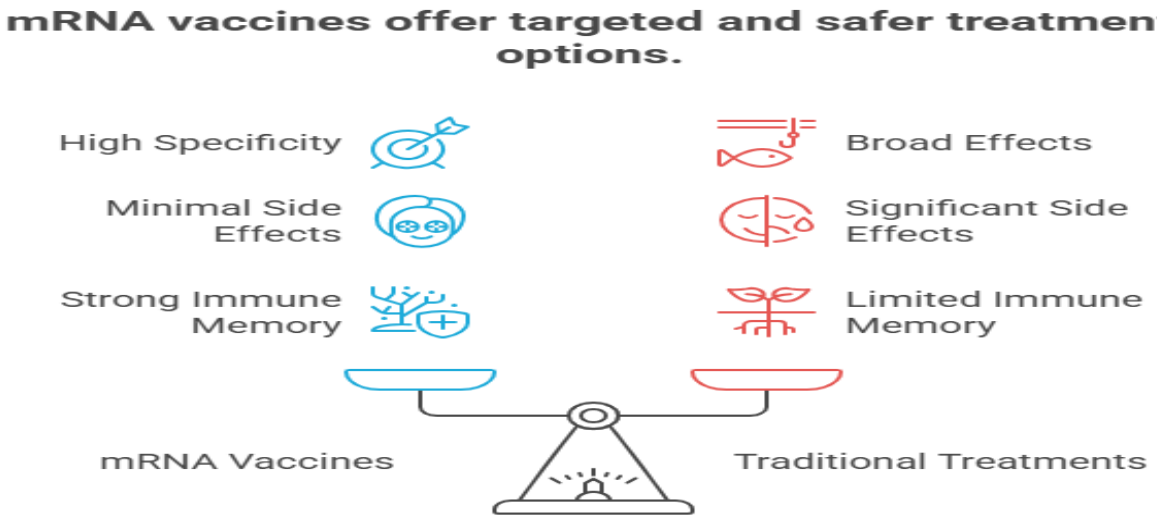

Fig.4 Advantages of mRNA vaccines over traditional treatments. Created by the author based on data from [8]

7. FUTURE DIRECTIONS

Basing on the success of the Phase I study, a Phase II clinical trial has already started, a project which is undertaken by Genentech, BioNTech, and Memorial Sloan Kettering, and on an international scale. The researchers intend to enroll 260 patients with pancreatic cancer in order to randomly allocate them to the old or the new protocol consisting of surgical resection plans, chemo-based medicines, and immunotherapeutics based on mRNA. The main aim is to determine whether this vaccine-induced technique provides better results compared to those of the existing standard treatment.

Effectively, the outcomes may even make it possible to gain regulatory approval and, ultimately, the prolonged adoption of custom mRNA shots. Simultaneously, the same research group at the Olayan Center for Cancer Vaccines, headed by Dr. Balachandran, is exploring parallel approaches with other resistant cancers, hence showing the broader possibilities of mRNA platforms in transforming oncology practices.[9]

Fig.5 Ongoing Phase 2 clinical trials and future directions of the mRNA vaccine Autogene Cevumeran. Created by the author based on data from). [9]

8. CONCLUSION

Modern medicine has to produce novel measures to respond to the threats that pancreatic cancer poses, and mRNA vaccines may be viewed as one of the strategies that can help overcome the current limitations of conventional approaches towards treating cancer. Smaller clinical trials are conducted to make sure there is acceptable safety profile as well as preliminary evidence of efficacy. The fast scale-up of mRNA preparations also makes such vaccines adaptive to the changing environment of pancreatic cancer. Based on the previous successes in infectious disease prevention, mRNA vaccines can redefine care against pancreatic cancer, improving survival, and overall quality of life. Ongoing studies are necessary to increase the access and maximise the effectiveness, translating into a paradigm shift in precision medicine.

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