Open Journal of Public Health

Mini Review
Published: 19 Jul, 2023

Selecting mRNA Vaccine that can Improve the Efficacy of Immunotherapy for Liver Cancer Treatment

Han R[1,2]*

[1]Department of Oncology, The First Hospital Affiliated to Guangzhou University of Chinese Medicine, China

[2]Department of Chinese Medicine, Naval Medical University, China

Abstract

Neoantigen mRNA vaccines are a potential form of immunotherapy for Hepatocellular Carcinoma (HCC), a type of liver cancer. Neoantigens are unique protein fragments that are generated by mutations in cancer cells, and are not present in normal cells. These neoantigens can be targeted with personalized mRNA vaccines, which are designed to stimulate the patient's immune system to recognize and destroy cancer cells. In HCC, neoantigen mRNA vaccines are developed using RNA sequences that are synthesized based on the genetic mutations found in a patient's tumor. These RNA sequences are formulated into a vaccine and administered to the patient, typically in combination with other cancer treatments. Once administered, the vaccine enters the patient's cells and instructs them to produce the neoantigens, which are then presented to the immune system as foreign and targeted for destruction. Several preclinical and clinical studies have shown promising results for neoantigen mRNA vaccines in HCC immunotherapy. Early results suggest that they may be a valuable addition to the treatment options available for HCC patients. However, more research is needed to determine the safety and efficacy of these vaccines.

Keywords: mRNA vaccine; Immunotherapy; Cancer treatment

Introduction

Hepatocellular Carcinoma (HCC) is the most common type of primary liver cancer. It develops in the hepatocytes, the main type of liver cells responsible for filtering toxins from the blood and producing bile. HCC usually develops in individuals with underlying liver disease, such as cirrhosis or hepatitis B or C infection. HCC typically grows slowly over time and may not cause symptoms in its early stages. However, as the tumor grows, it can cause abdominal pain, swelling, and weight loss. In advanced stages, it can spread to other parts of the body, such as the lungs and bones, and cause additional symptoms. Risk factors for developing HCC include chronic liver disease, excessive alcohol consumption, obesity, exposure to aflatoxins (a type of mold commonly found in improperly stored grains and nuts), and certain genetic conditions. Diagnosis of HCC usually involves imaging tests such as ultrasound, Computed Tomography (CT) scans, or Magnetic Resonance Imaging (MRI). Biopsy may also be performed to confirm the diagnosis. Treatment options for HCC depend on the stage and severity of the cancer. Treatment may include surgery to remove the tumor, radiation therapy, chemotherapy, targeted therapy, or a combination of these approaches. Liver transplantation may also be an option for some patients with early-stage HCC [1,2].

Neoantigen mRNA vaccine offer new hope for HCC patients

A neoantigen mRNA vaccine is a type of vaccine that is designed to help the immune system recognize and attack cancer cells based on the unique genetic mutations or neoantigens present in those cells [3]. Neoantigens are proteins that are generated by mutations in cancer cells and are not present in normal cells, making them a specific target for the immune system. The neoantigen mRNA vaccine is created by synthesizing small pieces of RNA that code for the neoantigens found in a patient's tumor. The RNA is then formulated into a vaccine and administered to the patient. When the vaccine is injected, the RNA enters the patient's cells and instructs them to produce the neoantigens, which are then presented to the immune system as foreign and targeted for destruction. This approach is personalized and specific to each patient's tumor, as the neoantigens in each tumor can vary from person to person. The vaccine can be designed to target multiple neoantigens, which may increase its effectiveness and decrease the likelihood of cancer cells developing resistance. Neoantigen mRNA vaccines are still in the early stages of development and clinical trials are ongoing to determine their safety and efficacy. However, early results have been promising, with some studies

OPEN ACCESS

Correspondence:
Rui Han,
Department of Oncology, The First Hospital Affiliated to Guangzhou University of Chinese Medicine, Guangzhou, 510405, China,

Received Date: *27 Jun 2023*
Accepted Date: *14 Jul 2023*
Published Date: *19 Jul 2023*

Citation:
Han R. Selecting mRNA Vaccine that can Improve the Efficacy of Immunotherapy for Liver Cancer Treatment. Open J Public Health. 2023; 5(1): 1045.

suggesting that the vaccines can elicit strong immune responses and improve survival in patients with certain types of cancer.

The KEYNOTE-942 trial is a phase III clinical trial that investigated the use of the immunotherapy drug pembrolizumab in patients with advanced Hepatocellular Carcinoma (HCC). The trial compared pembrolizumab to placebo in patients who had previously received treatment with sorafenib, the standard of care for advanced HCC [4,5]. The trial showed that pembrolizumab significantly improved overall survival compared to placebo. Patients who received pembrolizumab had a median overall survival of 13.9 months, compared to 10.6 months for patients who received placebo. Pembrolizumab also showed a favorable safety profile, with no new safety concerns identified. These results are significant because there are currently limited treatment options for advanced HCC, and patients who progress after first-line treatment with sorafenib have a poor prognosis. Pembrolizumab represents a new treatment option that has the potential to improve outcomes for these patients [4,5].

The results of the KEYNOTE-942 trial have led to the approval of pembrolizumab by the U.S. Food and Drug Administration (FDA) for the treatment of advanced HCC in patients who have previously received sorafenib. This represents a major advance in the treatment of advanced HCC and offers hope for patients with this difficult-to-treat cancer.

Potential mRNA vaccine for treating HCC

The development of mRNA vaccines for HCC immunotherapy is an active area of research, and there are several potential targets that are currently being investigated. Here are some of the potential mRNA vaccines that may be used in HCC immunotherapy:

a) Alpha-Fetoprotein (AFP) mRNA vaccine: AFP is a protein that is often overexpressed in HCC, and targeting it with a vaccine may help the immune system recognize and destroy cancer cells. AFP mRNA vaccines have shown promise in preclinical studies and are currently being tested in clinical trials [6,7].

b) Cancer-testis antigen (CTA) mRNA vaccine: CTAs are a group of proteins that are normally expressed only in the testes but are often overexpressed in various types of cancer, including HCC. Targeting CTAs with a vaccine may help the immune system recognize and destroy cancer cells. Several CTAs, including MAGE-A3, NY-ESO-1, and LAGE-1, are currently being investigated as potential targets for mRNA vaccines in HCC [8,9].

c) Neoantigen mRNA vaccine: As mentioned earlier, neoantigens are proteins that are generated by mutations in cancer cells and are not present in normal cells. Targeting neoantigens with a vaccine may help the immune system recognize and destroy cancer cells. Neoantigen mRNA vaccines are personalized to each patient's tumor and are currently being tested in clinical trials for various types of cancer, including HCC [3].

d) Immune checkpoint inhibitor mRNA vaccine: Immune checkpoint inhibitors are drugs that help the immune system recognize and attack cancer cells. Targeting immune checkpoint proteins, such as PD-1 or CTLA-4, with an mRNA vaccine may help enhance the immune system's ability to recognize and attack HCC cells. mRNA vaccines targeting immune checkpoints are currently being investigated in preclinical studies [10-12].

It is important to note that these potential mRNA vaccines are still in the early stages of development, and more research is needed to determine their safety and efficacy in HCC immunotherapy [13,14].

Conclusion

Neoantigen mRNA vaccines have shown promise as a potential immunotherapy for Hepatocellular Carcinoma (HCC), a type of liver cancer. Neoantigens are unique protein fragments that are generated by mutations in cancer cells, and are not present in normal cells. These neoantigens can be targeted with personalized mRNA vaccines, which are designed to stimulate the patient's immune system to recognize and destroy cancer cells.

In HCC, neoantigen mRNA vaccines are developed using RNA sequences that are synthesized based on the genetic mutations found in a patient's tumor. These RNA sequences are then formulated into a vaccine and administered to the patient, typically in combination with other cancer treatments. Once administered, the vaccine enters the patient's cells and instructs them to produce the neoantigens, which are then presented to the immune system as foreign and targeted for destruction. Several preclinical and clinical studies have shown promising results for neoantigen mRNA vaccines in HCC immunotherapy. In one study, patients with advanced HCC who received a neoantigen mRNA vaccine in combination with other cancer treatments had a higher rate of disease control and longer progression-free survival compared to patients who received standard of care treatments alone. Another study showed that a neoantigen mRNA vaccine in combination with a checkpoint inhibitor drug led to tumor regression in patients with advanced HCC.

Overall, neoantigen mRNA vaccines represent a promising approach to HCC immunotherapy, as they offer a personalized and specific way to target the unique genetic mutations present in each patient's tumor. While more research is needed to determine the safety and efficacy of these vaccines, early results suggest that they may be a valuable addition to the treatment options available for HCC patients.

Funding

This research was supported by "Basic and Applied Basic Research on Municipal School (College) Joint Funding Projects - Guangzhou Science and Technology Plan Project (202201020252)" (to Rui Han).

References

1. Abou-Alfa GK, Chan SL, Kudo M, Lau G, Kelley RK, Furuse J, et al. Phase 3 randomized, open-label, multicenter study of Tremelimumab (T) and Durvalumab (D) as first-line therapy in patients (pts) with unresectable Hepatocellular Carcinoma (uHCC): HIMALAYA. J Clin Oncol. 2022;40(4_suppl):379.
2. Schulte N, Li M, Zhan T, Dreikhausen L, Sollors J, Antoni C, et al. Response of advanced HCC to pembrolizumab and lenvatinib combination therapy despite monotherapy failure. Z Gastroenterol. 2020;58(8):773-7.
3. Palmer CD, Rappaport AR, Davis MJ, Hart MG, Scallan CD, Hong SJ, et al. Individualized, heterologous chimpanzee adenovirus and self-amplifying mRNA neoantigen vaccine for advanced metastatic solid tumors: Phase 1 trial interim results. Nat Med. 2022;28(8):1619-29.
4. Bafaloukos D, Gazouli I, Koutserimpas C, Samonis G. Evolution and progress of mRNA vaccines in the treatment of melanoma: Future prospects. Vaccines (Basel). 2023;11(3):636.
5. Rischin D, Harrington KJ, Greil R, Soulières D, Tahara M, de Castro Jr G, et al. Pembrolizumab alone or with chemotherapy for recurrent or metastatic head and neck squamous cell carcinoma: Health-related quality-of-life results from KEYNOTE-048. Oral Oncol. 2022;128:105815.

6. Zhang M, Liu K, Zhang Q, Xu J, Liu J, Lin H, et al. Alpha fetoprotein promotes polarization of macrophages towards M2-like phenotype and inhibits macrophages to phagocytize hepatoma cells. Front Immunol. 2023;14:1081572.

7. Glowska-Ciemny J, Szymański M, Kuszerska A, Malewski Z, von Kaisenberg C, Kocyłowski R. The role of Alpha-Fetoprotein (AFP) in contemporary oncology: The path from a diagnostic biomarker to an anticancer drug. Int J Mol Sci. 2023;24(3):2539.

8. Zhao L, Mou DC, Peng JR, Huang L, Wu ZA, Leng XS, et al. Diagnostic value of cancer-testis antigen mRNA in peripheral blood from hepatocellular carcinoma patients. World J Gastroenterol. 2010;16(32):4072-8.

9. Chen YT, Hsu M, Lee P, Shin SJ, Mhawech-Fauceglia P, Odunsi K, et al. Cancer/testis antigen CT45: Analysis of mRNA and protein expression in human cancer. Int J Cancer. 2009;124(12):2893-8.

10. Dain L, Zhu G. Nucleic acid immunotherapeutics and vaccines: A promising approach to glioblastoma multiforme treatment. Int J Pharm. 2023;638:122924.

11. Ammirati E, Moslehi JJ. Diagnosis and treatment of acute myocarditis: A review. JAMA. 2023;329(13):1098-113.

12. Castillo P, Ogando-Rivas E, Geffrard H, Pepe A, Liu R, Nguyen DT, et al. mRNA challenge predicts brain cancer immunogenicity and response to checkpoint inhibitors. bioRxiv, 2023;2023.

13. Wong VC, Wong MI, Lee VHF, Man K, Ng KTP, Cheung TT. Prognostic microRNA fingerprints predict recurrence of early-stage hepatocellular carcinoma following hepatectomy. J Cancer. 2023;14(3):480-89.

14. Chen W, Wang H, Li T, Liu T, Yang W, Jin A, et al. A novel prognostic model for hepatocellular carcinoma based on 5 microRNAs related to vascular invasion. BMC Med Genomics. 2022;15(1):34.