Trial record **9 of 93** for: mRNA for cancer

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Application of mRNA Immunotherapy Technology in Epstein-Barr Virus-related Refractory Malignant Tumors

ClinicalTrials.gov Identifier: NCT05714748

Recruitment Status : Recruiting
First Posted : February 6, 2023
Last Update Posted : February 6, 2023

See **Contacts and Locations**

View this study on Beta.ClinicalTrials.gov

Sponsor:
West China Hospital

Information provided by (Responsible Party):
Xingchen Peng, West China Hospital

Study Description

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Brief Summary:

The purpose of this study is to evaluate the efficacy and safety of mRNA vaccine for the EBV-positive Advanced Malignant Tumors.

Condition or disease	Intervention/treatment	Phase
Malignant **Tumors**	Biological: EBV mRNA vaccine	Phase 1

Detailed Description:

Epstein-Barr virus (Epstein-Barr virus), also known as human herpesvirus type 4, has an infection rate of over 90% in the population. The global disease burden caused by EBV infection is enormous, and it was one of the first human cancer viruses to be identified. Prophylactic EBV vaccines have the potential to significantly reduce the incidence or severity of EBV-associated diseases. Epstein-Barr virus is associated with a variety of tumors of epithelial and lymphoid origin, such as Burkitt's lymphoma, Hodgkin's lymphoma, nasopharyngeal carcinoma of epithelial origin, and some gastric cancers.

Vaccination is the most effective way to prevent EBV infection. In 1973, Epstein and Achong first proposed the basic principle of developing a vaccine against Epstein-Barr virus. However, more than 40 years later, there is still no approved EBV vaccine. Therefore, it is urgent to develop new drugs for the treatment of EBV. EBV usually lurks in human normal epithelial cells and B lymphocytes, shuttles between B lymphocytes and epithelial cells, and spreads continuously in the human body[2], leading to the recurrence of malignant tumors such as nasopharyngeal carcinoma, gastric cancer, and lymphoma with transfer. It can be seen that the development of therapeutic drugs that directly target EBV is expected to achieve better therapeutic effects on EBV-related malignant tumors. At present, new biological treatment strategies targeting EBV have shown good therapeutic potential in nasopharyngeal carcinoma, infectious mononucleosis, lymphoma and other EBV-related diseases in the clinical trial stage, including viral vector vaccines, DC or CAR -T cell therapy. At present, the virus vector preparations targeting EBV include Ankara vaccinia virus and adenovirus. These viruses have safety risks of integrating into the host genome and causing genome mutations in patients. The DC (Dendritic cell) or CAR-T cell therapy strategy targeting EBV is complicated to operate, takes a long time, is difficult to control quality, is difficult to produce on a

large scale, and has high production costs. In conclusion, the design strategy of the above-mentioned new biological therapy still has a high risk of difficult clinical or market transformation; therefore, it is necessary to develop new therapeutic biological agents targeting EBV.

mRNA vaccines are a promising new approach to cancer. Its working principle is: introduce the mRNA encoding the antigen into the cells of the body (especially the antigen-presenting cells), synthesize the antigen protein or polypeptide through the expression system of the host cell, activate cellular immunity and humoral immunity, and achieve the purpose of highly effective anticancer[13]. The mRNA does not need to enter the nucleus, it can be translated in the cytoplasm, and the effect is rapid; there is no risk of integration into the host genome, and it will be automatically degraded in the body, which is safe. Compared with traditional protein/polypeptide preparations, mRNA nucleic acid has no problems such as antigen conformation change and degradation, and has the advantages of long-term expression and persistent presentation of antigen; at the same time, it can simulate the natural infection process of the virus to activate the immune system and stimulate more Strong immune response; in addition, the production of mRNA preparations is simple and the synthesis is fast. Different mRNA preparations can be prepared using the same production steps and facilities, saving production costs. It is considered to be a new type of nucleic acid preparation with good clinical application prospects.

Based on the previous work, this project intends to carry out the research on new immunotherapy technology of "targeting EB virus mRNA nucleic acid to treat EBV-related malignant tumors". At present, there is no similar treatment method or product report in the world, which is very innovative and advanced. Therefore, this project intends to carry out phase I clinical research on the basis of previous research, in order to obtain a therapeutic candidate vaccine targeting EBV with independent intellectual property rights.

Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	9 participants
Allocation:	N/A
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	A Phase I Study of **mRNA** Vaccine for Patients With EBV-positive Advanced Malignant **Tumors**
Actual Study Start Date :	November 18, 2022
Estimated Primary Completion Date :	January 2024
Estimated Study Completion Date :	January 2025

Resource links provided by the National Library of Medicine NIH NLM

MedlinePlus related topics: Vaccines

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: Treatment Cohort With 20ug as the starting point, the dose was increased using a dose escalation scheme. Each subject only received one corresponding dose, and intramuscular injection was administered again every 7 days, and after 4 doses, the 5th dose was given after 1 month interval.	Biological: EBV mRNA vaccine With 20ug as the starting point, the dose was increased using a dose escalation scheme. Each subject only received one corresponding dose, and intramuscular injection was administered again every 7 days, and after 4 doses, the 5th dose was given after 1 month interval

Outcome Measures

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Primary Outcome Measures :

1. Adverse events [Time Frame: up to 12 months]

   Adverse events defined as the number of participants with adverse events according

2. Objective response rate [Time Frame: up to 12 months]

   ORR is defined as the percentage of patients who achieve a response, which can either be complete response (complete disappearance of lesions) or partial response (reduction in the sum of maximal tumor diameters by at least 30% or more)

3. Progress-Free Survival [Time Frame: up to 12 months]

   PFS is defined as the time from the administration of the first dose to first disease

4. Overall Survival [Time Frame: up to 12 months]

   OS is defined as the time from the administration of the first dose to death.

Eligibility Criteria

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Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years to 70 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	No

Criteria

Inclusion Criteria:

1. Male or female patients: ≥18 years old and ≤70 years old.
2. Patients with EBV-positive advanced malignant tumors after failure of second-line standard therapy.
3. ECOG physical condition score: 0-1 point.
4. Expected survival period ≥ 3 months.
5. The main organs are in good function, that is, the relevant inspection indicators within 14 days before randomization meet the following requirements:
    a. Blood routine examination: hemoglobin ≥ 90g/L and neutrophil count > 1.5×109/L and platelet count ≥ 80×109/L.
    b. Biochemical examination: total bilirubin≤1.5×ULN (upper limit of normal value), blood alanine aminotransferase (ALT) or blood aspartate aminotransferase (AST)≤2.5×ULN. if there is liver metastasis, ALT or AST≤5×ULN. Endogenous creatinine clearance ≥ 60ml/min (Cockcroft-Gault formula).
    c. Cardiac Doppler ultrasound evaluation: left ventricular ejection fraction (LVEF) ≥ 50%.
6. Sign the written informed consent
    a. Subjects must sign and date the EC-approved written informed consent in accordance with the guidelines of the competent authority and the research institution. Informed

consent must be signed prior to any protocol-related procedures that are not part of the subject's routine medical care.

b. Subjects must be willing and able to comply with the scheduled visits, treatment plans, laboratory tests, and other requirements of the study.

Exclusion Criteria:

Patients who meet any of the following criteria cannot be enrolled:

1. Participated in other drug clinical trials within 4 weeks;
2. The patient has a history of other tumors, unless it is cervical cancer in situ, treated skin squamous cell carcinoma or bladder epithelial tumor or other malignant tumors that have received radical treatment (at least 5 years before enrollment);
3. There are clinical symptoms or diseases of the heart that cannot be well controlled, such as: heart failure above NYHA grade 2, unstable angina, myocardial infarction within 1 year, clinically significant supraventricular or ventricular arrhythmia requiring treatment or intervention of patients.
4. For female subjects: pregnant or lactating women.
5. Patients have active pulmonary tuberculosis, bacterial or fungal infection (≥2 grades of NCI-CTCAE 5.0); HIV infection, active HBV infection, HCV infection.
6. Those who have a history of psychotropic drug abuse and cannot quit or have mental disorders;
7. The subject has any active autoimmune disease or has a history of autoimmune disease (such as the following, but not limited to: uveitis, enteritis, hypophysitis, nephritis, hyperthyroidism, hypothyroidism; the subject suffers from Subjects with vitiligo or asthma that had been completely remitted in childhood and who did not require any intervention in adulthood could be included; subjects with asthma requiring medical intervention with bronchodilators could not be included).
8. Any abnormalities or permanent body art (such as tattoos) at the inoculation site that, in the opinion of the investigator, would prevent observation of local reactions at the inoculation site.
9. Patients who have been vaccinated with mRNA drugs.
10. Have participated in clinical trials involving lipid nanoparticles (one of the components of the vaccine in this study).
11. There are contraindications for intramuscular injection
12. History of drug abuse or known medical, psychological or social conditions, such as history of alcohol or drug abuse.
13. Known allergy, hypersensitivity or intolerance to the research vaccine (including any excipients). There is a history of severe allergy to any drug, food, or vaccination, such as anaphylactic shock, allergic laryngeal edema, allergic dyspnea, allergic purpura,

thrombocytopenic purpura, local allergic necrotic reaction (Arthus reaction), etc.

14. From the screening period to 12 months after the full injection of the drug, the female subject has a pregnancy plan or the partner of a male subject has a pregnancy plan.
15. According to the investigator's judgment, there are concomitant diseases that seriously endanger the patient's safety or affect the patient's completion of the study.

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT05714748***

Contacts

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Locations

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Sponsors and Collaborators

West China Hospital

Investigators

Principal Investigator: Peng Xingchen West China Hospital

More Information

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Publications:

Balfour HH Jr, Schmeling DO, Grimm-Geris JM. The promise of a prophylactic Epstein-Barr virus

vaccine. Pediatr Res. 2020 Jan;87(2):345-352. doi: 10.1038/s41390-019-0591-5. Epub 2019 Oct 3.

Young LS, Yap LF, Murray PG. Epstein-Barr virus: more than 50 years old and still providing surprises. Nat Rev Cancer. 2016 Dec;16(12):789-802. doi: 10.1038/nrc.2016.92. Epub 2016 Sep 30.

Saha A, Kaul R, Murakami M, Robertson ES. Tumor viruses and cancer biology: Modulating signaling pathways for therapeutic intervention. Cancer Biol Ther. 2010 Nov 15;10(10):961-78. doi: 10.4161/cbt.10.10.13923. Epub 2010 Nov 15.

Tsao SW, Tsang CM, To KF, Lo KW. The role of Epstein-Barr virus in epithelial malignancies. J Pathol. 2015 Jan;235(2):323-33. doi: 10.1002/path.4448.

ERLAY J EM, LAM F, et al. Global Cancer Observatory: cancer today . Lyon, France: International Agency for Research on Cancer 2018 https://gcoiarcfr/today (accessed November 11th, 2020). 2018.

Iizasa H, Nanbo A, Nishikawa J, Jinushi M, Yoshiyama H. Epstein-Barr Virus (EBV)-associated gastric carcinoma. Viruses. 2012 Dec;4(12):3420-39. doi: 10.3390/v4123420.

Qiao YW, Zhao XQ, Liu J, Yang WJ. Clinicopathological features of Epstein-Barr virus-associated gastric carcinoma: A systematic review and meta-analysis. J BUON. 2019 May-Jun;24(3):1092-1099.

Ribeiro J, Malta M, Galaghar A, Afonso LP, Libanio D, Medeiros R, Dinis-Ribeiro M, Pimentel-Nunes P, Sousa H. Epstein-Barr virus is absent in gastric superficial neoplastic lesions. Virchows Arch. 2019 Dec;475(6):757-762. doi: 10.1007/s00428-019-02670-1. Epub 2019 Nov 1.

Taylor GS, Jia H, Harrington K, Lee LW, Turner J, Ladell K, Price DA, Tanday M, Matthews J, Roberts C, Edwards C, McGuigan L, Hartley A, Wilson S, Hui EP, Chan AT, Rickinson AB, Steven NM. A recombinant modified vaccinia ankara vaccine encoding Epstein-Barr Virus (EBV) target antigens: a phase I trial in UK patients with EBV-positive cancer. Clin Cancer Res. 2014 Oct 1;20(19):5009-22. doi: 10.1158/1078-0432.CCR-14-1122-T. Epub 2014 Aug 14.

Hui EP, Taylor GS, Jia H, Ma BB, Chan SL, Ho R, Wong WL, Wilson S, Johnson BF, Edwards C, Stocken DD, Rickinson AB, Steven NM, Chan AT. Phase I trial of recombinant modified vaccinia ankara encoding Epstein-Barr viral tumor antigens in nasopharyngeal carcinoma patients. Cancer Res. 2013 Mar 15;73(6):1676-88. doi: 10.1158/0008-5472.CAN-12-2448. Epub 2013 Jan 24.

Si Y, Deng Z, Lan G, Du H, Wang Y, Si J, Wei J, Weng J, Qin Y, Huang B, Yang Y, Qin Y. The Safety and Immunological Effects of rAd5-EBV-LMP2 Vaccine in Nasopharyngeal Carcinoma Patients: A Phase I Clinical Trial and Two-Year Follow-Up. Chem Pharm Bull (Tokyo). 2016;64(8):1118-23. doi: 10.1248/cpb.c16-00114.

Chia WK, Wang WW, Teo M, Tai WM, Lim WT, Tan EH, Leong SS, Sun L, Chen JJ, Gottschalk S, Toh HC. A phase II study evaluating the safety and efficacy of an adenovirus-DeltaLMP1-LMP2 transduced dendritic cell vaccine in patients with advanced metastatic nasopharyngeal carcinoma. Ann Oncol. 2012 Apr;23(4):997-1005. doi: 10.1093/annonc/mdr341. Epub 2011 Aug 4.

Nishikawa J, Yoshiyama H, Iizasa H, Kanehiro Y, Nakamura M, Nishimura J, Saito M, Okamoto T, Sakai K, Suehiro Y, Yamasaki T, Oga A, Yanai H, Sakaida I. Epstein-barr virus in gastric carcinoma. Cancers (Basel). 2014 Nov 7;6(4):2259-74. doi: 10.3390/cancers6042259.

Reinhard K, Rengstl B, Oehm P, Michel K, Billmeier A, Hayduk N, Klein O, Kuna K, Ouchan Y, Woll S, Christ E, Weber D, Suchan M, Bukur T, Birtel M, Jahndel V, Mroz K, Hobohm K, Kranz L, Diken M, Kuhlcke K, Tureci O, Sahin U. An RNA vaccine drives expansion and efficacy of claudin-CAR-T cells against solid tumors. Science. 2020 Jan 24;367(6476):446-453. doi: 10.1126/science.aay5967. Epub 2020 Jan 2.

Wang F, Qin Z, Lu H, He S, Luo J, Jin C, Song X. Clinical translation of gene medicine. J Gene Med. 2019 Jul;21(7):e3108. doi: 10.1002/jgm.3108. Epub 2019 Jul 15.

Fenton OS, Kauffman KJ, McClellan RL, Kaczmarek JC, Zeng MD, Andresen JL, Rhym LH, Heartlein MW, DeRosa F, Anderson DG. Customizable Lipid Nanoparticle Materials for the Delivery of siRNAs and mRNAs. Angew Chem Int Ed Engl. 2018 Oct 8;57(41):13582-13586. doi: 10.1002/anie.201809056. Epub 2018 Sep 14.

Miao L, Li L, Huang Y, Delcassian D, Chahal J, Han J, Shi Y, Sadtler K, Gao W, Lin J, Doloff JC, Langer R, Anderson DG. Delivery of mRNA vaccines with heterocyclic lipids increases anti-tumor efficacy by STING-mediated immune cell activation. Nat Biotechnol. 2019 Oct;37(10):1174-1185. doi: 10.1038/s41587-019-0247-3. Epub 2019 Sep 30.

Hou X, Zhang X, Zhao W, Zeng C, Deng B, McComb DW, Du S, Zhang C, Li W, Dong Y. Author Correction: Vitamin lipid nanoparticles enable adoptive macrophage transfer for the treatment of multidrug-resistant bacterial sepsis. Nat Nanotechnol. 2020 Jul;15(7):615. doi: 10.1038/s41565-020-0675-8.

Responsible Party:	Xingchen Peng, professor, West China Hospital
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First Posted:	February 6, 2023 Key Record Dates
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Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD: No

Studies a U.S. FDA-regulated Drug Product: No
Studies a U.S. FDA-regulated Device Product: No

Keywords provided by Xingchen Peng, West China Hospital:

mRNA vaccine
EBV
malignant **tumor**
immunotherapy

Additional relevant MeSH terms:

Neoplasms