

Research Progress of Novel Coronavirus Pneumonia Vaccine

Song Peng*

History and Public Administration School, Yancheng Teachers University, Yancheng, P. R. China

Abstract

Since novel coronavirus pneumonia (novel coronavirus pneumonia) novel coronavirus outbreak, countries around the world have accelerated the development of a new coronavirus pneumonia vaccine (new crown vaccine). As of December 2020, 60 candidate new coronal vaccines have been approved for clinical trials, among which 7 vaccines (3 inactivated vaccines, 2 mRNA nucleic acid vaccines, and 2 vector vaccines) have been approved for emergency use or conditional marketing. In this paper, the development progress, advantages, and disadvantages of six new coronal vaccines including inactivated vaccine, nucleic acid vaccine, vector vaccine, protein subunit vaccine, live attenuated vaccine and virus-like particle vaccine was reviewed. The results of the novel coronavirus pneumonia in phase III clinical trials show that the new vaccine has good safety and immunogenicity. The approved vaccine has been proved to have good protective efficacy. However, attention should be paid to the adverse reactions of the vaccine and the long-term protective effect.

Keywords: Novel coronavirus • Novel coronavirus pneumonia • Vaccine • Clinical trial • Research progress

Introduction

The novel coronavirus pneumonia (novel coronavirus pneumonia) has been raging around the world. As of December 2020, about 80000000 people were infected and about 1700000 died [1]. The novel coronavirus pneumonia vaccine (novel coronavirus pneumonia) has become an important strategy for controlling the new crown pneumonia epidemic situation due to the lack of effective treatment. The novel coronavirus (new crown virus) is a single strand positive RNA envelope virus. Its receptor binding region (spike binding, domain, and RBD) exposed on the surface of the protein S protein and S protein is the main target of the new crown vaccine design. In March 2020, the new coronal vaccine based on adenovirus vector in China and mRNA technology platform in the United States will be the first to enter clinical trials, followed by DNA vaccine and inactivated vaccine. As of December 2020, 60 vaccine candidates based on six different technical routes including inactivated vaccine, nucleic acid vaccine (including DNA vaccine and mRNA vaccine), vector vaccine, protein subunit vaccine, live attenuated vaccine and virus-like particle vaccine have been approved for clinical trials, and some vaccines have been approved for conditional marketing or emergency use. In this paper, the development progress, advantages and disadvantages, and challenges of the new crown vaccine were reviewed to provide a reference for follow-up research and immune strategy.

Literature Review

Progress in research and clinical trials

According to the statistics of the World Health Organization (who), as of December 2020, there are 60 new crown vaccines in clinical trials, including 8 inactivated vaccines, 15 nucleic acid vaccines (8 DNA vaccines and 7 mRNA vaccines), 16 vector vaccines (10 non-replicating virus vector

vaccines and 6 replicating virus vector vaccines), and 18 protein subunit vaccines. There were 2 virus-like particle vaccines and 1 live attenuated vaccine [2,3]. According to the clinical stage, there were 11 phases III clinical trials, 4 phase II / III clinical trials, 3 phase II clinical trials, 22 phases I / II clinical trials, and 20 phases I clinical trials. Among the 15 vaccines in phase III (including phase II / III) clinical trials, there were 4 inactivated vaccines and 4 non-replicating vector vaccines, 3 mRNA vaccines, 2 protein subunit vaccines, 1 DNA vaccine, and 1 virus-like particle vaccine [3]. In China, there are five new coronal vaccines in phase III clinical trials, including three inactivated vaccines, one adenovirus vector vaccine, and one protein subunit vaccine [3].

Inactivated vaccine

Inactivated vaccine adopts the traditional vaccine development process. Its principle is to use physical or chemical methods to inactivate the infectious complete virus after the virus is amplified and cultured, to make it lose pathogenicity and retain immunogenicity [4]. The inactivated vaccine can increase immunogenicity by adding adjuvants, which has the advantages of the simple production process, mature preparation and industrialization technology platform, good stability, safe use, controllable quality standards, etc. [5]. However, it needs to increase the number of inoculants to maintain immunogenicity [6], which requires a higher level of biological safety in the inactivation process and production process [7]. Three new coronal inactivated vaccines developed in China were approved for clinical trials in April 2020. The results of phase I/II clinical trials showed that the positive conversion rate of neutralizing antibody was more than 90% after two doses of vaccine, and the antibody level of 28- or 21-days interval was slightly higher than that of 14 days interval. The main adverse reactions were pain at the injection site, mild to moderate fever, mild self-limiting, and no serious abnormal reactions occurred [8-9]. On June 23, 2020, China launched the world's first international phase III clinical trial of a new crown inactivated vaccine in Abu Dhabi, United Arab Emirates; in July, another two international phases III clinical trials of the inactivated vaccine developed by China were conducted in Brazil, United Arab Emirates, Turkey, and other places respectively, and were approved for emergency vaccination. On December 9 and 13, an inactivated vaccine developed in China was officially registered in the United Arab Emirates and Bahrain [10]. On December 30, the State Drug Administration approved the conditional marketing of China's first Xinguan inactivated vaccine. The analysis of the novel coronavirus pneumonia vaccine showed that the vaccine was safe

*Address for Correspondence: Peng S, History and Public Administration School, Yancheng Teachers University, Yancheng, P. R. China, E-mail: songp@yctu.edu.cn

Copyright: © 2021 Peng S. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Received 23 January 2021; **Accepted** 05 February 2021; **Published** 12 February 2021

after vaccination. The 2 times of the vaccine had high titer antibody, and the positive rate of neutralizing antibody was 99.52%, and the protective efficacy for new crown pneumonia was 79.34% [11]. An inactivated vaccine developed in India entered phase III clinical trial on November 11 [3].

Nucleic acid vaccine

The nucleic acid vaccine is a new technology for vaccine development in recent years, including DNA vaccine and mRNA vaccine. Its mechanism is to construct DNA plasmid or mRNA fragment *in vitro* as an immunogen and introduce it into the human body through plasmid injection or mRNA nanoparticles to synthesize protein antigen *in vivo* and induce immune response [12,13]. Compared with traditional vaccine development technologies such as a live attenuated vaccine, inactivated vaccine, and recombinant vaccine, the nucleic acid vaccine has the advantages of low transmission risk, rapid and flexible construction, easy mass production, and low production cost, but it has the disadvantages of integrating into the body's own nuclear DNA (DNA vaccine), easy degradation and strict storage and transportation temperature requirements (mRNA vaccine) [14,15]. In the past, no nucleic acid vaccine has been licensed and approved for human use, only nucleic acid vaccines that have entered the clinical research stage, such as HIV vaccine, rabies vaccine, and Zika virus vaccine [13]. In November 2020, the United States announced that two phases III clinical trials of the new coronal mRNA vaccine have reached the endpoint requirements of the main efficacy, with the protective efficacy of 94.1% and 95.0% respectively. The efficacy of the new coronal mRNA vaccine is consistent for different ages, gender, and ethnic groups, and it also has a protective effect on the elderly [16,17]. Data showed that the novel coronavirus pneumonia vaccine produced a high level of antibody after the first doses of mRNA vaccine decreased slightly over time. However, after 3 months of booster immunization (second doses), the antibody level of all subjects still increased, and the neutralizing antibody produced was higher than that of durability of responses after SARS-CoV-2 mRNA-1273 vaccination [18].

The common adverse reactions included pain, fatigue, headache, and fever at the injection site, and no serious safety problems related to the vaccine were found [16,17]. According to the US Food and Drug Administration (FDA), idiopathic facial paralysis occurred in four phase III subjects who were vaccinated with mRNA vaccine, but there is no clear evidence to show its association with the vaccine [19]. In December 2020, MHRA, Health Canada, and FDA successively approved the emergency use of two new coronal mRNA vaccines [20]. In addition, the new coronal mRNA vaccine developed by the German Curevac company has entered phase II / III clinical trials, and the new coronal mRNA vaccine developed in China is currently in phase I clinical stage [3]. The first new coronal DNA vaccine to enter clinical trials was developed by an American company. The phase I clinical trial was launched in April 2020, and the phase II phase of phase II/III clinical trial was entered in November 2020 [21]. The vaccine was injected intradermally with a handheld intelligent device. The results of phase I clinical trial showed that 94% of the subjects showed complete immune response at the 6th week after vaccination. After 8 weeks, the vaccine was confirmed to be safe and tolerable, and no serious adverse reactions were reported [22,23].

Vector vaccine

Vector vaccine is constructed by inserting protective antigens into other specific viral or bacterial vectors (such as adenovirus, influenza virus, Salmonella, etc.). Viral vector vaccines can be divided into replicative and replication-deficient (i.e. non-replicative) viral vectors according to whether they can produce living offspring viruses [24]. The vector vaccine vector is rich in sources, easy to produce and prepare, and can stimulate humoral and cellular immunity at the same time. The dosage is small, the immunogenicity is close to nature, and the vector itself can play an adjuvant effect. However, the pre-storage of vector virus-related antibody in the human body has a certain impact on the vaccination effect [25,26]. The recombinant Ebola virus disease vaccine (adenovirus vector) developed in China was approved by the State Drug Administration for new drug registration in 2017 [24]. The Ebola virus vaccine rVSV-ZEBOV with vesicular stomatitis virus as the vector has been approved by

the EU and FDA for emergency use in the case of an Ebola outbreak in the Democratic Republic of Congo [27]. Other virus vector vaccines are still in clinical trials. 4 novel coronavirus pneumonia carrier vaccines have been introduced into the third phase clinical trials in China, Britain, Russia, and the United States respectively, all of which are non-replicating viral vector vaccines. The results of the phase II clinical trial of the non-replicating adenovirus vector vaccine in China showed that after 28 days of full-dose and half-dose inoculation, the positive conversion rates of RBD antibody against RBD region of virus S protein were 96% and 97% respectively.

The common adverse reaction was fever (8% in the full-dose group and 1% in a half-dose group), and no serious adverse reaction was reported [28]. The one-dose vaccination scheme of the vaccine has entered phase III trials in Argentina, Chile, Mexico, Pakistan, Russia, and other places, and phase II clinical trials with immunization procedures of two doses (56 days) have also been registered [3]. The mid-term analysis of phase III clinical trial of the vector vaccine developed in the UK showed that the protective effect was 62.1% for the subjects receiving two full doses, 90% for the subjects receiving half dose+full dose, and 70.4% for the comprehensive protective effect; the serious adverse event rates reported by the vaccine group and the control group were 0.7% and 0.7% respectively 8%, no serious adverse events related to the vaccine were found, and the vaccine was approved for emergency use in the UK in December 2020 [29]. The immunization procedure of the vector vaccine developed by Russia is two doses, with an interval of 21 days. The interim data of the phase III clinical trial shows that the effective rate of the vaccine is 91.4% 28 days after the first dose, and the effective rate of the vaccine is more than 95% 49 days after the first dose. There is no adverse reaction other than the solicitation event, and it has been approved for emergency marketing in Belarus, Argentina, Kazakhstan, and other countries [30]. The early clinical trial of the vector vaccine developed in the United States found that the effect of two doses is better than that of one dose, and the effect of the 8-week interval is better than that of the 4-week interval. The phase III clinical trial of two doses with an 8-week interval was launched in November 2020 [31].

Protein subunit vaccine

Protein subunit vaccine is a kind of vaccine made from recombinant virus target antigen gene constructed on the expression vector and then transformed into bacteria, yeast, mammalian, or insect cells to induce the expression of antigen protein. The protein subunit vaccines on the market include influenza vaccine, hepatitis B vaccine, etc. Two new corona protein subunit vaccines developed in the United States and China have entered phase III clinical trials. The vaccine developed in the United States is made of recombinant protein nanoparticles vaccine technology and adjuvant. Its phase I/II clinical trials show that most subjects have no or slight adverse reactions, with a short duration of fewer than 2 days on average. The most common systemic reactions are joint pain and fatigue. The adjuvant can enhance immune response and induce Th1 cell response. The dosage of adjuvant is 5 μ g twice. Novel coronavirus pneumonia patients were found to have higher levels of anti S protein IgG antibody and neutralizing antibody than those of most new crown pneumonia patients in the convalescent stage. In the adjuvant group was higher than that in the other groups. The vaccine developed in China has selected the dimerized RBD region of S protein as the antigen target. Phase I/II clinical trials have been completed and phase III clinical trials are being carried out. The most common adverse reactions were pain and swelling at the injection site, and the incidence of fever and fatigue was lower than that of other new coronal vaccines (such as mRNA vaccine and adenovirus vector vaccine). In novel coronavirus pneumonia, the neutralizing antibody levels were higher than those. Safety and immunogenicity data support the phase III clinical trial using 25 μ g, three-dose vaccination procedure to further large-scale evaluation of safety and efficacy.

Live attenuated vaccine

Live attenuated vaccine is to deal with pathogens and make them

mutate. Through passage culture, we can obtain pathogen mutants with reduced toxicity or even non-toxicity and retain immunogenicity. Inoculating live virus mutants into the human body will not cause disease but can induce an immune response. The live attenuated vaccines on the market include BCG, polio, mumps, Japanese encephalitis, and hepatitis A [32]. As of December 2020, the live attenuated coronavirus vaccine jointly developed by the United States and India has entered phase I clinical trial [3].

Virus like particle vaccine

Virus Like Particle (VLP) is a highly structured hollow particle which is self-assembled by one or several capsid proteins of virus in a heterologous system and has the same or similar structure as natural virus particles but does not contain viral genetic material. The VLP vaccines on the market include human papillomavirus vaccine and hepatitis B vaccine. VLP vaccine is an empty shell protein structure, which does not contain genetic material, and has no infectivity and replication ability. Due to its spatial structure like natural virus particles, VLP vaccine can present multiple and high-density antigen epitopes, effectively induce cellular and humoral immunity. The vaccine developed in Canada has entered phase II/III clinical trials, and the vaccine jointly developed by Australia and India has entered phase I/II clinical trials [3]. The phase I clinical trial of the vaccine developed in Canada used two kinds of adjuvants to test the candidate vaccine. The mid-term analysis results showed that the vaccine with VLP adjuvant was well tolerated; after the subjects were inoculated with two doses of adjuvant containing vaccine, they all produced obvious antibody and cellular immunity, and the antibody in the lowest dose group with adjuvant was 10 times higher than that in the convalescent serum.

Advantages and disadvantages of different new crown vaccine development technology routes

Safety: The safety of the new crown vaccines which have entered stage III is good, but there are some differences in theory between different vaccines. Inactivated vaccine and protein subunit vaccine will not cause virus infection, but live attenuated vaccine needs to reproduce in vivo, which has the risk of virulence reversion infection or transmission. Therefore, the safety of inactivated vaccine and protein subunit vaccine is higher than that of live attenuated vaccine, and the composition of protein subunit vaccine is more accurate, and the safety is slightly higher than that of inactivated vaccine. DNA vaccines in nucleic acid vaccines have the risk of integrating exogenous DNA into the host genome after entering the body, resulting in oncogene activation, or inactivation of tumor suppressor genes, or chromosomal instability [12]; synthetic raw materials and wrapping materials used in the synthesis of mRNA vaccines may have toxicity and may cause apoptosis of surrounding host cells [32]. The non-replicating adenovirus vector vaccine cannot self-replicate and has good safety. However, due to the wide range of adenovirus infection and lack of targeting, the adenovirus vector may infect other normal tissue cells while infecting target organs and target cells, resulting in adverse reactions. In addition, attention should be paid to Antibody-Dependent Infection Enhancement (ADE), especially in inactivated vaccines. Although no new coronal vaccine-related ADE has been reported, similar phenomena have been observed in the Middle East Respiratory Syndrome (MERS) candidate vaccine and Severe Acute Respiratory Syndrome (SARS) candidate vaccine. According to the results of phase I/II clinical trials, the vaccines of all technical routes were well tolerated, and the main adverse reactions were pain, redness, swelling, fatigue, and fever at the injection site. The fever after injection of adenovirus vector vaccine and mRNA vaccine was more obvious than that of inactivated vaccine and protein subunit vaccine [8-32]. In phase III clinical trial, most of the adverse reactions of each route vaccine were mild and there was no confirmed serious safety event related to the vaccine.

Effectiveness: In the target product profile of the new crown vaccine, who proposed that the protective efficacy of the new crown vaccine should be at least 50%, and more than 70% is more acceptable, and the efficacy can be evaluated according to the endpoint of "illness, severe illness and/or detoxification/transmission ability". Among the four vaccines with published

efficacy, the inactivated vaccine has a protective effect of 79.34%, vector vaccine 62%-90%, and mRNA vaccine more than 90%, all of which meet the requirements. However, in a novel coronavirus pneumonia pandemic, it is not suitable to evaluate or directly compare the clinical efficacy. Because the different clinical research designs and research sites of different vaccines are different, the results will be different. The real protective effect of vaccines needs to be obtained by an epidemiological study of subsequent large-scale phase IV trials or extensive vaccination.

Technology maturity: Inactivated vaccine and live attenuated vaccine are the first generations vaccine technology, while protein subunit vaccine and VLP vaccine are the second generation vaccine technology. A variety of vaccines based on these technology platforms have been put on the market with high technology maturity [32]. For viral vector vaccine, many research and development units have a certain foundation for vaccine construction and clinical trials [24], and the technology maturity is medium. As a relatively new vaccine development technology, the nucleic acid vaccine only has a DNA vaccine for horses, salmon, dogs, pigs, and other animals [12]. Previously, the nucleic acid vaccine for human disease prevention has not been put on the market, and the technology maturity is not high [32]. There is still a lack of process data and quality control standards after nucleic acid enters the human body.

Storage and transportation: Because the mRNA is unstable and easy to degrade, the mRNA vaccine has high requirements for storage conditions. One mRNA vaccine developed by the United States and Germany needs to be stored at -70°C, and the thawed vaccine vial can only be stored for 5 days under cold storage (2-8°C); the other mRNA vaccine can only be stable for 30 days under 2-8°C, and needs to be stored at -20°C. DNA vaccine has a stable structure and relatively good thermal stability. The developer said that it can be stable at room temperature for more than one year without freezing [21]. An inactivated vaccine has good thermal stability and can be stored at 2-8°C. The protein subunit vaccine can be stored at 2-8°C for more than 6 months and kept stable at room temperature and 40°C for at least 1 month. The storage conditions of the vector vaccine are convenient and flexible, which can be stored in 4°C liquid buffer or the form of lyophilized powder for more than one year [32].

Production capacity: Due to the need for a virus culture process, the production of inactivated vaccine and attenuated vaccine requires a high level of biological safety and a long production cycle, which makes it difficult to enlarge the production capacity [32]. After the production process of the protein subunit vaccine is determined, it is easy to mass-produce, and the production capacity is higher than that of the traditional vaccine development platform [32]. Viral vector vaccine can be cultured in suspension cells on a large scale, with relatively low production cost. Compared with traditional vaccine development technology, the production capacity of viral vector vaccine is improved, and it is easy to achieve mass production [24]. The nucleic acid vaccine does not rely on cell expansion, so it is simple to construct, easy to achieve mass production, and the production speed is fast [13].

US companies that produce mRNA vaccines are expected to supply 1.3 billion doses by the end of 2021. Oxford, UK, is expected to produce 3 billion doses of vector vaccine in 2021 [26]. The U.S. protein subunit vaccine company plans to increase its global production capacity to more than 2 billion doses per year. The vaccine development and production enterprises of various technical routes in China have made great efforts to increase production capacity and have already met the conditions for large-scale production. The production capacity of two inactivated vaccines in China is expected to reach 1 billion doses in 2021, the annual production capacity of protein subunit vaccine is expected to reach 300 million doses, and the annual production capacity of five vaccine enterprises undergoing phase III clinical trials will reach 2 billion doses.

Challenges and Prospects

Since 2020, with the joint efforts of all countries, we have quickly mastered

the genomic characteristics, pathogenesis, and infection mechanism of the new coronavirus, and made full use of mature or emerging biotechnology to realize the rapid development of the vaccine. However, it takes 10-15 years for the traditional vaccine development technology, and only 10% of the clinical vaccines can be approved for marketing. In addition to the inherent shortcomings of the above vaccines, the following concerns or difficulties need to be solved in the follow-up use: (1) the clinical trial time is short, the sample size is limited, and rare adverse events (such as 1/10) cannot be observed (2) because all age groups are susceptible to NCV, there is no research report on NCV vaccination for children, adolescents and people with underlying diseases, so the key to form a population immune barrier and block transmission is to realize whole population vaccination; (3) NCV is a single strand positive chain RNA. The virus can mutate continuously in the occurrence and development of epidemic situation, and there are many blind spots in its infection and immune mechanism, so there are still uncertain factors in the protective efficacy and immune persistence of the vaccine currently developed.

Conclusion

China has joined the global "new crown vaccine implementation plan" to promote the fair distribution of vaccines in the world. While ensuring the provision of vaccines to developing countries, China has also led more countries in a position to support the plan. The novel coronavirus pneumonia is expected to be effective in controlling the spread of the new crown pneumonia epidemic with the help of the new crown vaccine. The vaccine development and application experience will also be applied to more infectious disease prevention vaccine development and prevention and control and open a new era of vaccine to protect human health.

References

- Nadia, Jebri. "World Health Organization Declared a Pandemic Public Health Menace: A Systematic Review of the Coronavirus Disease 2019 "COVID-19." SSRN 138 (2019): 437-439.
- Lianpan Dai and George F. Gao. "Viral Targets for Vaccines against COVID-19." *Nat Rev Immunol* 21 (2021): 73-82.
- Jozef Bartovic, Siddharta Sankar Datta, Santino Severoni and Veronika D'Anna. "Ensuring Equitable Access to Vaccines for Refugees and Migrants during the COVID-19 Pandemic." *WHO* 99 (2021): 3.
- Deng Qiang, Wang Zichen and Wu Qin. "Advances in Novel Coronavirus Vaccines." *J Jinan Uni* 41 (2020): 511-519.
- Mulligan, Mark. "An Inactivated Virus Candidate Vaccine to Prevent COVID-19." *JAMA* 324 (2020): 943-945.
- Simran Preet Kaur and Vandana Gupta. "COVID-19 Vaccine: A Comprehensive Status Report." *Virus Res* 288 (2020): 1-7.
- Zhen Yongsu and Zhao Kai. "Vaccine Research and Application." *People Health* 13 (2013): 1.
- Shengli Xia, Yuntao Zhang, Yanxia Wang and Hui Wang, et al. "Safety and Immunogenicity of an Inactivated SARS-CoV-2 Vaccine, BBIBP-CorV : A Randomised, Double-Blind, Placebo-Controlled, Phase 1/2 Trial." *Lancet Infect Dis* 21 (2020): 39-51.
- Zhiwei Wu, Yaling Hu, Miao Xu and Zhen Chen, et al. "Safety, Tolerability and Immunogenicity of an Inactivated SARS-CoV-2 Vaccine in Healthy Adults Aged 18-59 Years: A Randomised, Double-Blind, Placebo-Controlled, Phase 1/2 Clinical Trial." *Lancet Infect Dis* 21 (2020): 181.
- Jerome Amir, Singh. "UAE Ministry of Health and Prevention announces official registration of inactivated COVID-19 Vaccine used in Humanity Trials." *Epidemiol Int* 5 (2020): 27.
- Fred, Gray. "Consumption: Council House Management." *State Hous Br* 28 (2021): 196-232.
- Michele A. Kutzler and David B. Weiner. "DNA Vaccines: Ready for Prime Time." *Nat Rev Genet* 98 (2008): 776-788.
- Norbert Pardi, Michael J. Hogan, Frederick W. Porter and Drew Weissman, et al. "mRNA Vaccines: A New Era in Vaccinology." *Nat Rev Drug Discov* 17 (2018): 261-279.
- John J. Suschak, James A. Williams and Connie S. Schmaljohn. "Advancements in DNA Vaccine Vectors, Non-Mechanical Delivery Methods and Molecular Adjuvants to Increase Immunogenicity." *Human Vacc Immunother* 13 (2017): 2837-2848.
- John R. Mascola and Anthony S. Fauci. "Novel Vaccine Technologies for the 21st Century." *Nat Rev Immunol* 20 (2020): 87-88.
- Fernando P. Polack, Stephen J. Thomas, Nicholas Kitchin and Judith Absalon, et al. "Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine." *N Engl J Med* 383 (2020): 2603-2615.
- Lindsey R. Baden, Hana M. El Sahly, Brandon Essink and Karen Kotloff, et al. "Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine." *N Engl J Med* 30 (2020): 02.
- Alicia T. Widge, Nadine G. Roupheal, Lisa A. Jackson and Evan J. Anderson, et al. "Durability of Responses after SARS-CoV-2 mRNA-1273 Vaccination." *N Engl J Med* 384 (2021): 80-82.
- Cheng Chuangang, Mu Ting and Yuan Jun. "Research Progress of Recombinant Viral Vector Vaccine." *Chinese J Viral Dis* 8 (2018): 318-328.
- Liu, Yunfan. "Construction of a New Replication Defective Adenovirus Vector System." *Dis Control Prevent* 7 (2011): 45.
- Feng-Cai Zhu, Xu-Hua Guan, Yu-Hua Li and Jian-Ying Huang, et al. "Immunogenicity and Safety of a Recombinant Adenovirus Type-5-Vectored COVID-19 Vaccine in Healthy Adults Aged 18 Years or Older : A Randomised, Double-Blind, Placebo-Controlled, Phase 2 trial." *Lancet* 396 (2020): 479-488.
- Gavin, Koh. "Safety and Efficacy of the ChAdOx1 nCoV-19 Vaccine (AZD1222) Against SARS-CoV-2: An Interim Analysis of Four Randomised Controlled Trials in Brazil South Africa and the UK." *Lancet* 397 (2020): 99-111.
- Song Quanwei and Wang Huaqing. "Novel Coronavirus Vaccine Characteristics and Research Progress under Different Technological Routes." *Chinese Med J* 38 (2020): 3030-3040.
- Cheryl Keech, Gary Albert, Iksung Cho and Andrea Robertson, et al. "Phase 1-2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine." *N Engl J Med* 24 (2020): 2320-2332.
- Li, Yanlin. "Research Progress on Immune Mechanism and Application of Virus like Particle Vaccine." *Int J Biol Prod* 42 (2019): 203-208.
- Guo Huimin, Miao Qihong and Tan Yonggui. "Common Expression Systems and Application Progress of Virus Like Particles." *Chinese J Animal Infect Dis* 25 (2017): 82-86.
- Anurodh Shankar Agrawal, Xinrong Tao, Abdullah Algaissi and Tania Garron, et al. "Immunization with Inactivated Middle East Respiratory Syndrome Coronavirus Vaccine Leads to Lung Immunopathology on Challenge with Live Virus." *Human Vacc Immunother* 12 (2016): 2351-2356.
- Yushun Wan, Jian Shang, Shihui Sun and Wanbo Tai, et al. "Molecular Mechanism for Antibody-Dependent Enhancement of Coronavirus Entry." *J Virol* 94 (2020): 45.
- Feng-Cai Zhu, Yu-Hua Li, Xu-Hua Guan and Li-Hua Hou, et al. "Safety, Tolerability and Immunogenicity of a Recombinant Adenovirus Type-5 Vectored COVID-19 Vaccine A Dose-Escalation, Open-Label, Non-Randomised, First-In-Human Trial." *Lancet* 395 (2020): 1845-1854.

30. Meryn Voysey and Andrew J. Pollard. "Safety and Immunogenicity of the ChAdOx1 nCoV-19 Vaccine against SARS-CoV-2: A Preliminary Report of a Phase Single-Blind, Randomised Controlled Trial." *Lancet* 396 (2020): 467-478.
31. Tung Thanh Le, Zacharias Andreadakis, Arun Kumar and Raúl Gómez Román, et al. "The COVID-19 Vaccine Development Landscape." *Nat Rev Drug Discov* 19 (2020): 305-306.
32. Nathan D. Grubaugh, William P. Hanage and Angela L. Rasmussen. "Making Sense of Mutation: What D614G Means for the COVID-19 Pandemic Remains Unclear." *Cell* 182 (2020): 794-795.

How to cite this article: Song Peng.. Research Progress of Novel Coronavirus Pneumonia Vaccine." *Clin Case Rep* 11 (2021): 1421