Research, Society and Development, v. 9, n. 12, e20191211123, 2020
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v9i12.11123

Nano COVID-19 Vaccines: the firsts RNA lipid nanoparticle vaccines being approved from history - Review

Nano Vacinas COVID-19: as primeiras vacinas de nanopartículas de lipídios de RNA sendo aprovadas na história - Revisão

Nano vacunas COVID-19: las primeras vacunas de nanopartículas lipídicas de ARN siendo aprobadas en la historia – Revisión

Received: 12/11/2020 | Reviewed: 12/13/2020 | Accept: 12/16/2020 | Published: 12/19/2020

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Abstract

A new coronavirus, identified in Wuhan, China, has spread globally, infecting millions of people and causing significant morbidity and mortality. The pandemic state, declared by the World Health Organization on March 11, 2020, transformed the world and made people adapt to social distance to control the spread of the virus. The race against time in search of therapeutic solutions has become essential, and nanotechnology may be able to make vaccines available in record time to stimulate the immunization of individuals. Since the beginning of 2020, scientists and companies are rapidly advancing to make vaccine candidates available at a different rate compared to other pandemics that have existed. This review briefly presents the pros and cons of the third generation vaccines, Moderna / NIAID and Pfizer - BioNTech, which are in phase 3 tests, based on lipid RNA nanoparticles. Great collaborative efforts are being invested so that soon the world population will receive doses of vaccines with proven

efficacy and enable increased survival, since the pandemic has already caused many irreversible losses.

Keywords: COVID-19; Coronavirus; Vaccine; Nanomedicine; Nanotechnology.

Resumo

Um novo coronavírus, identificado em Wuhan, China, se espalhou globalmente, infectando milhões de pessoas e causando morbidade e mortalidade significativas. O estado de pandemia, declarado pela Organização Mundial da Saúde em 11 de março de 2020, transformou o mundo e fez com que as pessoas se adaptassem ao distanciamento social para controlar a disseminação do vírus. A corrida contra o tempo em busca de soluções terapêuticas tornou-se imprescindível, e a nanotecnologia pode conseguir disponibilizar vacinas em tempo recorde para estimular a imunização dos indivíduos. Desde o início de 2020, os cientistas e empresas estão avançando rapidamente para disponibilizar vacinas candidatas num ritmo diferenciado comparado a outras pandemias que existiram. Esta revisão apresenta, brevemente, os prós e contras das vacinas de terceira geração, Moderna / NIAID e Pfizer - BioNTech, que estão em testes de fase 3, com base em nanopartículas de RNA lipídico. Grandes esforços colaborativos estão sendo investidos para que em breve a população mundial receba doses de vacinas com eficácia comprovada e possibilite o aumento da sobrevida, visto que a pandemia já ocasionou muitas perdas irreversíveis.

Palavras-chave: COVID-19; Coronavírus; Vacina; Nanomedicina; Nanotecnologia.

Resumen

Un nuevo coronavirus, identificado en Wuhan, China, se ha propagado a nivel mundial, infectando a millones de personas y provocando una morbilidad y mortalidad significativas. El estado pandémico, declarado por la Organización Mundial de la Salud el 11 de marzo de 2020, transformó el mundo e hizo que las personas se adaptaran a la distancia social para controlar la propagación del virus. La carrera contrarreloj en busca de soluciones terapéuticas se ha vuelto fundamental, y la nanotecnología puede hacer que las vacunas estén disponibles en un tiempo récord para estimular la inmunización de los individuos. Desde principios de 2020, los científicos y las empresas están avanzando rápidamente para que los candidatos a vacunas estén disponibles a un ritmo diferente en comparación con otras pandemias que han existido. Esta revisión presenta brevemente los pros y los contras de las vacunas de tercera generación, Moderna / NIAID y Pfizer - BioNTech, que se encuentran en pruebas de fase 3, basadas en nanopartículas de ARN lipídico. Se están invirtiendo grandes esfuerzos de

colaboración para que pronto la población mundial reciba dosis de vacunas de probada eficacia y permitan una mayor supervivencia, ya que la pandemia ya ha provocado muchas pérdidas irreversibles.

Palabras clave: COVID-19; Coronavirus; Vacuna; Nanomedicina; Nanotecnología.

1. Introduction

In December 2019 an outbreak of an unknown disease emerged in Wuhan, China, it was later discovered that it was caused by a new coronavirus, which was named SARS-COV-2 and, consequently, could cause coronavirus disease (COVID -19), responsible for causing the World Health Organization (WHO) to declare a new outbreak pandemic on March 11, 2020, after the disease had spread intercontinentally (Cucinotta & Vanelli, 2020)

There have been several attempts to find an effective treatment against COVID-19 since then, however most of the results have been discouraging and other controversial. Even unveiling some mechanisms involving COVID-19, the scenario is still quite challenging (Pacheco et al., 2020).

However, after a year of anxious waiting, agony and millions of deaths from coronavirus disease, phase 3 experiments on some vaccines have finally been completed. We highlight here mainly the vaccine from Pfizer – BioNTech and Moderna/NIAID, both using a lipid nanoparticle platform carrying the virus RNA. These vaccines revolutionized the world, first because they are the first third generation vaccines widely accepted, with results released in record time, and which promise to change the world pandemic scenario (Campos et al., 2020; Mahase, 2020b).

There are dozens of vaccines using nanoparticles in their methodology some using nanometric viruses or other nanoparticles. However, here we bring a comparison between the results of the most advanced third generation RNA lipid nanoparticle vaccines from Moderna/NIAID and Pfizer – BioNTech, with pros and cons, in addition to the challenges facing a pandemic that is not over yet, but which already sheds light on the end of the tunnel with the help of nanomedicine (Campos et al., 2020; Huang et al., 2020).

2. Methods

Studies published in PubMed, Scielo, and Google Scholar databases. According to the indexes of the various databases, search terms were used: “nanovaccines”, “COVID-19”, “Moderna/NIAID”, “Pfizer – BioNTech” without any language restrictions.

3. Nano Vaccines Candidates in Phase 3 for COVID-19

Moderna/NIAID vaccine

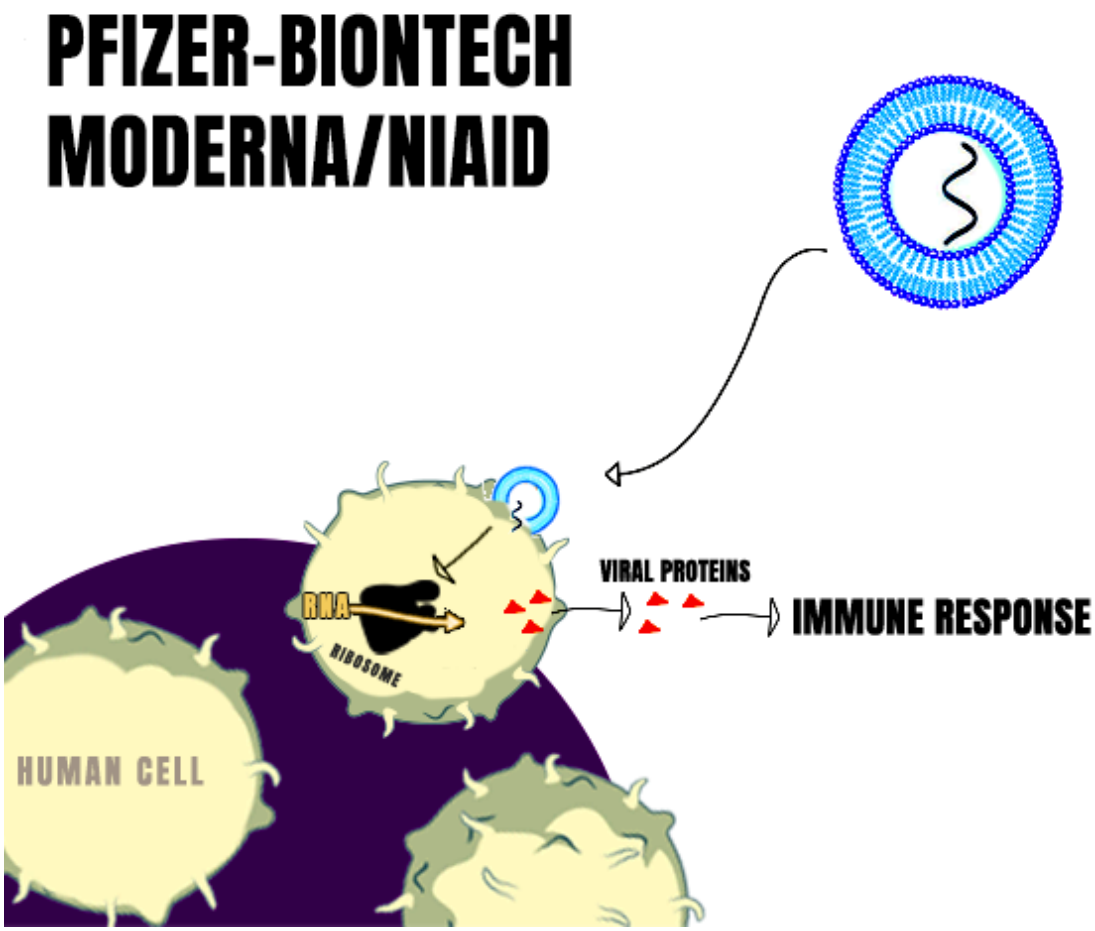
The Moderna/NIAID vaccine (mRNA-1273) works with mRNA, encapsulated by lipid nanoparticles (Figure 1), capable of encoding the coronavirus Spike protein and causing host cells to produce anti-Spike protein immune responses. This vaccine is administered in two doses, at an interval of 0-28 days, has an efficiency of 94.5% and is easily stored (-20ºC) (Jackson et al., 2020; Mahase, 2020b) (Table 1).

Pfizer–BioNTech vaccine

The Pfizer-Biotech vaccine is based on a modified virus mRNA platform carried by lipid nanoparticles (Figure 1). Initially Pfizer-BioNTech had released results of the BNT162b1 vaccine (which encodes for the S receptor-binding domain), however due to the better safety profile results of BNT162b2 (encoding for SARS-CoV-2 full-length S, stabilized in the prefusion conformation), this was chosen for phase 3 tests and achieved an efficiency of 95% (Mahase, 2020a; Mulligan et al., 2020; Polack et al., n.d.; Walsh et al., 2020) (Table 1).

This vaccine was first approved in the United Kingdom (UK), but despite having one of the best vaccine efficacies against COVID-19, has a limitation that can be a barrier for countries without structure: the vaccine has to be stored at temperatures below -70ºC (Mahase, 2020a) (Table 1).

Figure 1. Mechanism of RNA lipid nanoparticle vaccines from Moderna/NIAID and Pfizer-BioNTech. Lipid nanoparticles carrying mRNA coding spike protein that triggering immune response in host cells.



Source: Authors (2020).

Table 1. Comparison of Nano Vaccines candidates Moderna and Pfizer-BioNTech.

Company	Vaccine Name	Vaccine Type	Route of administration	Number of doses	Timing of doses	Storage	Value	Effective
Moderna/NIAID	mRNA-1273	LNP-encapsulated mRNA	IM	2	0-28 days	-Household fridge: 30 days; -Room temperature: 12 hours; - and -20°C: six months.	£ 25 per dose	94,5%
BioNTech/Fosun Pharma/Pfizer	BNT162b2	LNP-encapsulated mRNA	IM	2	0-28 days	*−70°C*	£15 per dose	95%

Source: Authors (2020).

4. Perspectives

Unlike vaccines with live or attenuated virus, RNA vaccines allow, for example, pregnant and immunocompromised women to take the vaccine, in addition to being a much faster alternative in production, when compared to traditional vaccines (Sahin et al., 2014).

Thanks to this technology, the long-awaited phase 3 vaccines have finally been completed, giving much hope to humanity in challenges with the COVID-19 pandemic. But there are still some questions that need to be answered: when will the entire world population have access to these and other vaccines against COVID-19? Will low income countries be able to buy vaccines? How long will these vaccines give an effective immune response? Will they be able to prevent the transmission of the virus? These and many other questions may be answered soon. But in the meantime, the vaccine must be applied in all possible ways, to mitigate the damage caused by this terrible disease (Mahase, 2020b).

However, it is unquestionable that the world has changed the way of producing vaccines, a process that would take years, which lasted about a year (Kim et al., 2020). Shi et al (2010) already stated that nanotechnology would revolutionize the world, and, in fact, changed in this pandemic. Thanks to mRNA technology vaccine and nanomedicine we can finally think of an end to a pandemic that has devastated many families (Shi et al., 2010).

5. Conclusion

About one year after the emergence of the new coronavirus (SARS-COV-2), phase 3 trials of innovative third generation vaccines were completed in record time, with the help of nanomedicine. Although Pfizer – BioNTech's nano vaccine is 95% effective and approved in the United Kingdom, it has logistical problems, as it needs a temperature below -70º to be stored, making it difficult to use in many countries. On the other hand, Moderna/NIAID nano vaccine has an efficiency of 94.5% and can be stored in conventional freezers (-20º), facilitating its use in several countries. Nanomedicine helped revolutionize history, in the battle against COVID-19, by producing 3rd generation vaccines, using lipid nanoparticles carrying RNA. For the first time in history, we will have vaccines of RNA with lipid nanoparticles approved and saving millions of lives.

Acknowledgements

The authors gratefully acknowledge financial support from: the Brazilian National Council for Technological and Scientific Development (CNPq), Coordinating Agency for Advanced Training of Graduate Personnel (CAPES), Foundation for Research Support of the Federal District (FAPDF) an the Dean of Research and Post-Graduation of the University of Brasília (DPP-UnB).

References

Campos, E. V. R., Pereira, A. E. S., De Oliveira, J. L., Carvalho, L. B., Guilger-Casagrande, M., De Lima, R., & Fraceto, L. F. (2020). How can nanotechnology help to combat COVID-19? Opportunities and urgent need. *Journal of Nanobiotechnology*, *18*(1), 1–23. https://doi.org/10.1186/s12951-020-00685-4

Cucinotta, D., & Vanelli, M. (2020). WHO declares COVID-19 a pandemic. *Acta Bio-Medica: Atenei Parmensis*, *91*(1), 157–160.

Huang, L., Rong, Y., Pan, Q., Yi, K., Tang, X., Zhang, Q., Wang, W., Wu, J., & Wang, F. (2020). SARS-CoV-2 vaccine research and development: conventional vaccines and biomimetic nanotechnology strategies. *Asian Journal of Pharmaceutical Sciences*.

Jackson, L. A., Anderson, E. J., Rouphael, N. G., Roberts, P. C., Makhene, M., Coler, R. N., McCullough, M. P., Chappell, J. D., Denison, M. R., Stevens, L. J., & others. (2020). An mRNA Vaccine against SARS-CoV-2—Preliminary Report. *New England Journal of Medicine*.

Kim, Y. C., Dema, B., & Reyes-Sandoval, A. (2020). COVID-19 vaccines: breaking record times to first-in-human trials. *Npj Vaccines*, *5*(1), 1–3.

Mahase, E. (2020a). *Covid-19: UK approves Pfizer and BioNTech vaccine with rollout due to start next week*. British Medical Journal Publishing Group.

Mahase, E. (2020b). *Covid-19: What do we know about the late stage vaccine candidates?*

British Medical Journal Publishing Group.

Mulligan, M. J., Lyke, K. E., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Neuzil, K., Raabe, V., Bailey, R., Swanson, K. A., Li, P., Koury, K., Kalina, W., Cooper, D., Fontes-Garfias, C., Shi, P. Y., Türeci, Ö., Tompkins, K. R., Walsh, E. E., … Jansen, K. U. (2020). Phase 1/2 study of COVID-19 RNA vaccine BNT162b1 in adults. *Nature*. https://doi.org/10.1038/s41586-020-2639-4

Pacheco, T. J. A., da Silva, F. de M., DE SOUZA, D. G., da Silva, V. C. M., & Faria, R. S. (2020). Coronavirus disease 2019 (COVID-19): Updated evidence of comparative overview, diagnosis and treatments. *Revista Cereus*, *12*(3), 228–243.

Polack, F. P., Thomas, S. J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J. L., Pérez Marc, G., Moreira, E. D., Zerbini, C., Bailey, R., Swanson, K. A., Roychoudhury, S., Koury, K., Li, P., Kalina, W. V, Cooper, D., Frenck, R. W., Hammitt, L. L., Gruber, W. C. (n.d.). Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*, *0*(0), null. https://doi.org/10.1056/NEJMoa2034577

Sahin, U., Karikó, K., & Türeci, Ö. (2014). mRNA-based therapeutics—developing a new class of drugs. *Nature Reviews Drug Discovery*, *13*(10), 759–780.

Shi, J., Votruba, A. R., Farokhzad, O. C., & Langer, R. (2010). Nanotechnology in drug delivery and tissue engineering: from discovery to applications. *Nano Letters*, *10*(9), 3223–3230.

Walsh, E. E., Frenck Jr, R. W., Falsey, A. R., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Neuzil, K., Mulligan, M. J., Bailey, R., & others. (2020). Safety and immunogenicity of two RNA-based COVID-19 vaccine candidates. *New England Journal of Medicine*.

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