Allergenic components of the mRNA-1273 vaccine for COVID-19: possible involvement of polyethylene glycol and IgG-mediated complement activation

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January 1, 2021

Abstract

Following the emergency use authorization of the vaccine mRNA-1273 on 18th December 2020 in the US and the vaccine BNT162b2 one week earlier, two mRNA vaccines are in currently used for the prevention of coronavirus disease 2019 (COVID-19). Phase 3 pivotal trials on both vaccines excluded individuals with a history of allergy to vaccine components. Immediately after the initiation of vaccination in the United Kingdom, Canada, and in the US, anaphylactic reactions have been reported. While the culprit trigger requires investigation, initial reports suggested the excipient polyethylene glycol 2000 (PEG-2000), which is contained in both vaccines as PEG-micellar carrier system as the potential culprit. Surface PEG chains form a hydrate shell to increase stability and prevent opsonization. Allergic reactions to such PEGylated lipids are rarely IgE-mediated, but may result from complement activation-related pseudoallergy (CARPA) that has been described to similar liposomes. In addition, mRNA-1273 also contains tromethamine (trometamol), which has been reported to cause anaphylaxis to e.g. gadolinium-based or iodinated contrast media. Skin prick-, intradermal-, epicutaneous- tests, in vitro sIgE assessment, evaluation of sIgG/IgM, as well as basophil activation test are in use to demonstrate allergic reactions to various components of the vaccines.

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BNT162b2 vaccine:

- Active component: mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2

Excipients:
- ALC-0315 = (4-hydroxybutyl) azanediyl]bis (hexane-1,6-diy]bis(2-hexy]decanate)
- ALC-0159 = 2-(polyethylene glycol) 2000 -N,N-diteradecylacetamide
- 1,2-distearoyl-sn-glycero-3-phosphocholine
- Cholesterol
- Potassium chloride
- Potassium dihydrogen phosphate
- Sodium chloride
- Disodium hydrogen phosphate dihydrate
- Sucrose
- Water for injections

mRNA-1273 vaccine:

- Active component: mRNA encoding the viral spike (S) glycoprotein of SARS-CoV-2

Excipients:
- SM-102
- 1,2-dimyristoyl-sn-glycero-3-methoxypolyethylene glycol-2000
- Cholesterol
- Tromethamine
- Tromethamine hydrochloride
- Acetic acid
- Sodium acetate
- Sucrose