Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Cystic Fibrosis 21 (2022) e173–e175

Contents lists available at ScienceDirect

Journal of Cystic Fibrosis

journal homepage: www.elsevier.com/locate/jcf

Safety of mRNA-based vaccines against SARS-CoV-2 in people with cystic fibrosis aged 12 years and over

Adverse reactions following the administration of mRNA-based vaccines against SARS-CoV-2 indicate acceptable safety profiles with recipients complaining mostly of local reactions which resolve in a few days [1]. However, mild forms of myocarditis and pericarditis also resolving without sequalae were reported in around 4 cases per 100,000 young males vaccinated and 0.5 per 100,000 women [2]. Severe reactions, including anaphylaxis, were rarely observed (less than 5 people per million vaccinated) mainly among women and individuals with a history of clinical allergy [3].

People affected by cystic fibrosis (pwCF), were among the first to receive anti-SARS-CoV-2 vaccines in several countries including Italy, due to their risk of developing severe Covid-19. However, there are no data on the safety of mRNA-based vaccines against SARS-CoV-2 in this population. Therefore, we conducted a study aimed at evaluating the reactogenicity and safety of these vaccines in pwCF.

All patients aged ≥12 years, in regular follow-up at the paediatric and adult CF centres of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan, who received at least one dose of the mRNA-based vaccines BNT162b2 (COMIRNATY BioNTech Manufacturing GmbH) or mRNA-1273 (SPIKEVAX Moderna Biotech Spain, S.L.) between March and October 2021 were asked to participate in this study.

Patients were subsequently interviewed by the attending physician of their CF centre in order to complete a diary card recording solicited local and systemic adverse reactions for 7 days after each administration. Severity of adverse reactions was graded using the following criteria: mild (transient or mild discomfort for <48 h, no interference with activity, and no medical intervention or therapy required), moderate (mild-to-moderate limitation in activity, and no or minimal medical intervention or therapy required), severe (substantial limitation in activity and medical intervention or therapy required), or potentially life-threatening (requiring assessment in emergency department or admission to hospital) [4]. All adverse events, even those apparently unrelated or with unclear link with the vaccination were also collected during the interview and at regular follow-up visits at the CF centres up to November 2021.

Data are presented as frequencies and percentage of patients reporting each reaction. Percentage of patients reporting any type of local and systemic reactions are provided with 95% confidence intervals (CIs) based on the binomial distribution. Frequencies of moderate adverse reactions were compared across age groups and according to respiratory function, organ transplant status, oxygen therapy and history of Covid-19.

The study was approved by the Ethics Committee of the IRCCS, Istituto Nazionale per le Malattie Infettive, Lazzaro Spallanzani, Rome, Italy (protocol number: 354 2020/2021) and patients signed the informed consent before being included in the study.

We enrolled 424 patients (median age: 28 years, interquartile range: 19-41, range: 12-81) who, at the time of the study, received the first dose of vaccine; 411 of them completed the two-dose course, whereas 13 patients did not receive the second dose due to previous SARS-CoV-2 infection within 12 months from the first dose; most patients received the BNT162b2 vaccine (N=379, 89.4%). Local reactions were reported by the majority of patients after either the first (82.8%, 95% CI: 78.8-86.3) or the second dose (75.9%, 95% CI: 71.5-80.0), while the frequency of systemic reactions was higher after receiving the second (60.3%, 95% CI: 55.4-65.1) as compared to the first dose (41.3%, 95% CI: 36.5-46.1) (Table 1). Three-quarters of the patients (N=321) complained of pain at the injection site after the first dose, while fatigue, headache, malaise and myalgia were the most frequent systemic reactions, reported in more than 10% of the patients. Similarly, after the second dose around 70% of the patients (N= 285) reported pain at the injection site, whereas systemic reactions were more frequently observed as compared to the first dose.

Most adverse reactions after both vaccine doses were considered of mild severity, while 94 (22.2%) reactions of moderate severity were reported after the first dose and 132 (31.1%) after the second dose. No significant differences were detected across age groups, transplant status, respiratory function categories, oxygen therapy and history of Covid-19 (Supplementary Table S1).

Despite the large imbalance between the number of patients receiving mRNA-1273 (N=45) and BNT162b2 vaccine (N=379), we did not observe less reactogenicity of BNT162b2, which on the contrary was reported by the US surveillance system v-safe [1], based on more than 3.6 million vaccine recipients. In fact, in our study the frequency and severity of adverse reactions to the first injection were similar between the two vaccines, while fewer adverse reactions were reported after the second injection of mRNA-1273 (local: 69.0% vs 76.7%, systemic: 45.2% vs 62.1%), although the differences were not statistically significant (Supplementary Table S2).

Our population included three patients with a history of severe anaphylactic reactions who received the vaccine in a protected environment and did not experience any severe reaction.

An acute coronary syndrome (ACS) episode was observed after 8 days from the second dose, in a patient aged 50 years with diabetes and hypertension who had a previous ACS in 2012. Given the pre-existing conditions, this event was considered unlikely related to the vaccine.

As of November 2021, we did not register any case of myocarditis or pericarditis as well as any anaphylactic reaction or other solicited adverse events. However, although including a relatively large number of patients, our study is not adequately powered to evaluate these rare events. Moreover, our results are limited to subject aged ≥12 years and to two doses of vaccine since at the

https://doi.org/10.1016/j.jcf.2022.02.009

Table 1
Number of people with cystic fibrosis reporting solicited local or systemic adverse reactions 0 to 7 days after the first and the second dose of mRNA-based vaccines against SARS-CoV-2.

	First dose		Second dose	
	Frequency	Percentage	Frequency	Percentage
No. of doses administered	424	100	411	100
Local reactions (Injection site)				
Any type	351	82.8	312	75.9
Pain	321	75.7	285	69.3
Sore arm	85	20.0	78	19.0
Swelling	35	8.3	35	8.5
Redness	24	5.7	14	3.4
Induration	23	5.4	25	6.1
Warmth	10	2.4	19	4.6
Itch	3	0.7	3	0.7
Hematoma	0	0	1	0.2
Systemic reactions				
Any type	175	41.3	248	60.3
Fatigue	74	17.5	106	25.8
Headache	65	15.3	82	20.0
Malaise	46	10.8	71	17.3
Myalgia	45	10.6	78	19.0
Fever	40	9.4	120	29.2
Joint pain	28	6.6	45	10.9
Chills	21	5.0	44	10.7
Nausea	8	1.9	20	4.9
Lymphadenopathy	5	1.2	10	2.4
Pulmonary exacerbations	2	0.5	11	2.7
Abdominal pain	1	0.2	6	1.5
Dizziness	1	0.2	3	0.7
Migraine with scotoma	1	0.2	0	0
Palpebral swelling	1	0.2	0	0
Skin rash	1	0.2	0	0
Diarrhoea	1	0.2	4	1.0
Vomit	0	0	2	0.5
Insomnia	0	0	2	0.5
Lumbago	0	0	1	0.2
Pharyngodynia	0	0	1	0.2

time of the study vaccines were not yet approved for younger children and the booster dose was not available.

Despite these limitations, this is the first work reporting on the safety of mRNA vaccines in a relatively large group of pwCF basically confirming what has been documented in the general population [1]. However, local reactions after the first dose were more frequently reported in our CF population as compared to what has been registered in the US surveillance data (82.8% vs 65.4% for the BNT162b2 vaccine) and the proportions of main systemic reactions were slightly lower after either the first or second dose [1]. In particular, fatigue was reported by 17.5% of our pwCF after the first dose and by 25.8% after the second dose, while corresponding figures observed in the US general population were 29.1% and 47.8%, respectively.

In conclusion, our results indicate that mRNA vaccines for pwCF are well-tolerated and safe in the short-term. Thus, the benefit of preventing severe Covid-19 outweigh the complains related to the mild-to-moderate adverse reactions observed.

Funding

None

Declaration of Competing Interest

None

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcf.2022.02.009.

CRediT authorship contribution statement

Gianfranco Alicandro: Conceptualization, Methodology, Formal analysis, Data curation, Visualization, Writing – original draft. **Valeria Daccó:** Investigation, Data curation, Writing – review & editing. **Lisa Cariani:** Investigation, Data curation, Writing – review & editing. **Martina Contarini:** Investigation, Data curation. **Letizia Corinna Morlacchi:** Investigation, Data curation. **Chiara Rosazza:** Investigation, Data curation. **Calogero Sathya Sciarrabba:** Investigation, Data curation. **Federica Ferraro:** Investigation, Data curation. **Chiara Lanfranchi:** Investigation, Data curation. **Beatrice Silvia Orena:** Investigation, Data curation. **Carla Colombo:** Conceptualization, Resources, Project administration, Writing – review & editing, Supervision.

References

[1] Chapin-Bardales J, Gee J, Myers T. Reactogenicity following receipt of mRNA-based Covid-19 vaccines. JAMA - J Am Med Assoc 2021;325:2201–2. doi:10.1001/jama.2021.5374.
[2] Witberg G, Barda N, Hoss S, Richter I, Wiessman M, Aviv Y, et al. Myocarditis after Covid-19 vaccination in a large health care organization. N Engl J Med 2021. doi:10.1056/nejmoa2110737.
[3] Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA Covid-19 vaccines in the US-December 14, 2020-January 18, 2021. JAMA - J Am Med Assoc 2021;325:1101–2. doi:10.1001/jama.2021.1967.

[4] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–15. doi:10.1056/nejmoa2034577.

Gianfranco Alicandro
Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Milan, Italy

Valeria Daccó
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Milan, Italy

Lisa Cariani
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Microbiology Unit, Milan, Italy

Martina Contarini, Letizia Corinna Morlacchi
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Respiratory Unit and Adult Cystic Fibrosis Centre, Milan, Italy

Chiara Rosazza, Calogero Sathya Sciarrabba, Federica Ferraro, Chiara Lanfranchi
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Milan, Italy

Beatrice Silvia Orena
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Microbiology Unit, Milan, Italy

Andrea Gramegna, Francesco Blasi
Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Respiratory Unit and Adult Cystic Fibrosis Centre, Milan, Italy

Carla Colombo*
Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy
Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Milan, Italy

*Corresponding author at: Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Cystic Fibrosis Centre, Via Della Commenda 9, 20122, Milan, Italy.
E-mail address: carla.colombo@unimi.it (C. Colombo)
Revised 11 February 2022