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Original article

Early tolerability of Comirnaty vaccine in patients with chronic neurological diseases

C. Budowski [a,b,*], C. Zavanone [a], L. Thivard [a], K. Vassilev [a], S. Dupont [a,b,c]

[a] Rehabilitation Unit, Hôpital de la Pitié-Salpêtrière, AP–HP, 47, boulevard de l'Hôpital, 75651 Paris cedex 13, France
[b] Sorbonne Université, Faculté de médecine, 91-105 boulevard de l'hôpital, 75013 Paris, France
[c] UMPC-UMR 7225 CNRS-UMRS 975 Inserm, Centre de recherche de l'Institut du Cerveau et de la Moelle Epinière (ICM), Paris, France

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ABSTRACT

Patients with chronic neurological diseases may have predisposing risk factors for severe COVID-19 and should be considered as priority candidates for SARS-CoV-2 vaccination. Nevertheless, the safety of RNA vaccine was evaluated in healthy volunteers or in patients with stable chronic medical conditions excluding patients with chronic neurological diseases. We report here the early tolerability of Comirnaty vaccine in 36 patients with chronic neurological diseases and demonstrate good early tolerability, better than found in healthy people in phase 3 trials.

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1. Introduction

The global pandemic of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) affected millions of persons worldwide. In December 2020, BionNTech and Pfizer launched a new mRNA-based vaccine: Comirnaty [1]. In France, this vaccine has been available since January 2021 in rehabilitation services [2]. Patients in neurological rehabilitation units often have predisposing risk factors for severe COVID-19 such as advanced age, cardiovascular comorbidity [3], or the neurological disease itself like brain tumour, stroke, or multiple sclerosis. Furthermore, SARS-CoV-2 infection may worsen the underlying chronic neurological disease. Therefore, these patients should be given priority for vaccination, which is why Comirnaty vaccine was systematically proposed to all the patients hospitalised in the neurological rehabilitation unit of the Pitié-Salpêtrière Hospital. We describe here the early tolerability of the vaccine in the first patients with chronic neurological diseases who underwent complete vaccination.

* *Corresponding author.*
E-mail address: clara.budowski@gmail.com (C. Budowski).
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2. Methods

We collected oral consent for each patient or from the trusted person if necessary. All patients were vaccinated by intramuscular injection in the arm. Hemiplegic patients were vaccinated in the contralateral non-plegic arm. Adverse events were systematically assessed in all patients 10 days after the vaccination according to the following list [4]: lymphadenopathy, anaphylaxis, insomnia, headache, facial paralysis, nausea, myalgia, joint pain, local reactions, pain at the injection site, fever and a category ''other''. Exclusion criteria were a previous recent (< 3 months) clinical or microbiologic diagnosis of COVID-19. Five patients declined vaccination.

3. Results

Between January 8th and February 26th, 36 patients were vaccinated: 35 received the two doses; one patient died from aspiration pneumonia complicated by atelectasis before the second injection. This patient had post-stroke swallowing difficulties and multiple comorbidities. His death was not related to the vaccination. The average length between the two injections was 28 days. Mean age of the patients was 69 ± 12 years. There were 22 men and 14 women. Neurological diseases are described in Table 1. Six patients had concomitant immunosuppressive treatments for their underlying neurological disease: temozolomide (4 patients); temozolo-

Table 1 – Clinical characteristics of patients and main side effects.

Age	Interdose (days)	Gender	Pathology	Adverse Events I	Adverse Events II
55	28	Male	Epilepsy	–	–
71	28	Male	Haemorrhagic stroke	–	–
62	28	Male	Haemorrhagic stroke	Myalgia, joint pain, insomnia and nausea	–
72	28	Female	Haemorrhagic stroke	–	–
67	28	Male	Haemorrhagic stroke	–	–
43	42	Female	Haematoma	Dizziness	headache, fatigue, pain at the injection site, insomnia
88	28	Male	Ischaemic stroke	Myalgia	–
76	28	Female	Ischaemic stroke	–	–
77	28	Female	Ischaemic stroke	Pain at the injection site	–
63	28	Male	Ischaemic stroke	–	–
62	28	Male	Ischaemic stroke	Pain at the injection site	–
46	28	Male	Ischaemic stroke	–	–
86	28	Female	Ischaemic stroke	–	–
83	28	Female	Ischaemic stroke	–	–
54	28	Female	Ischaemic stroke	Pain at the injection site	fever
73		Male	Ischaemic stroke	Vomiting	
86	28	Female	Ischaemic stroke	Fever	–
80	28	Male	Ischaemic stroke	–	–
58	28	Male	Ischaemic stroke	–	–
55	21	Female	Ischaemic stroke	–	–
56	28	Female	Demyelinating disease of the central nervous system	–	–
74	28	Male	Multiple sclerosis	–	–
80	21	Male	Parkinson's disease	–	–
84	21	Male	Parkinson's disease	Fatigue	–
86	28	Male	Parkinson's disease	–	–
81	21	Female	Parkinson's disease	–	–
68	28	Male	Progressive supranuclear palsy	Fatigue	–
48	28	Male	Thrombophlebitis	Myalgia, local haematoma	–
73	28	Female	Tuberculosis of the central nervous system	–	–
76	32	Male	Astrocytoma	–	–
61	28	Male	Glioblastoma	–	–
77	28	Female	Glioblastoma	–	–
69	28	Female	Glioblastoma	–	–
64	28	Male	Glioblastoma	–	–
75	28	Male	Primary central nervous system lymphoma	Local haematoma	–
77	26	Male	Primary central nervous system lymphoma	–	–

mide with bevacizumab (1 patient); rituximab, ifosfamide, carboplatine, and etoposide (1 patient).

No allergic reactions were noticed.

After the initial dose, adverse events were reported for 12 patients (33%). These events resolved quickly and only two patients experienced adverse events after the second dose (6%).

We distinguished local events from systemic events. Concerning local events, five patients reported adverse events after the first dose: three experienced pain (8%) and two (6%) developed a local haematoma at the injection site. All the symptoms, except the local haematoma related to thrombopaenia or anticoagulant therapy, lasted less than 24 hours. One patient had pain at the injection site after the second dose.

Concerning systemic events, eight patients (22%) reported systemic side effects after the first dose: myalgia ($n = 3$, 8%); fatigue ($n = 2$, 6%); nausea and/or vomiting ($n = 2$, 6%); fever, dizziness, joint pain, and insomnia ($n = 1$ each, 3%). After the second dose, only two patients reported adverse events which resolved in one day: respectively headache, asthenia, insomnia in one patient and fever in another one.

4. Discussion

In our study, a two-dose regimen of Comirnaty/BNT162b2 vaccine (30 μg per dose, given 28 days apart) was found to be safe in a brief follow-up period after the administration with even better tolerability than those found in the phase 2/3 trial assessing the safety, immunogenicity and efficacy of the vaccine [5].

In the phase 2/3 trial, 43,448 participants received either two 30 μg doses of BNT162b2 administered 21 days apart or placebo. Participants were all healthy adults or adults with stable chronic medical conditions including human immunodeficiency virus, hepatitis B virus, or hepatitis C virus infection. Compared to these participants, our patients were older (median age of 69 years old versus 55 years) with a larger proportion of men (61% vs. 50.6%), all exhibiting chronic neurological diseases. Like Polack et al. [5], we excluded patients with a medical history of COVID-19, but contrarily to that study we included patients receiving immunosuppressive therapy or having immunocompromising conditions such as multiple sclerosis or brain tumours. Six of our patients had concomitant immunosuppressive treatments including rituximab for one patient. The immune response to SARS-CoV-2 messenger RNA (mRNA) vaccines in patients treated by rituximab has been recently questioned by Boyarsky et al. who found that patients on rituximab were less likely to develop antibody response [6]. Nevertheless, we did not test our patients for SARS-CoV-2 antibodies and only report here data on early tolerability that was not modified by concomitant immunosuppressive treatments.

Globally, the tolerability was better in our patients with chronic neurological diseases than in healthy volunteers. Conversely to the phase 3 study, in our study the adverse events (local or systemic) were:

- more frequent after the first than the second dose and;
- not influenced by age.

4.1. *Local reactogenicity*

In Polack's study [5], mild-to-moderate pain at the injection site within seven days after an injection was the most commonly reported local reaction. Pain was less frequent among participants older than 55 years (71% after the first dose, 66% after the second dose) than among younger participants (83% after the first dose; 78% after the second dose). In general, local reactions were mild-to-moderate in severity and resolved within one to two days.

In our study, only four patients reported pain at the injection site (11%, 8% after the first dose; 3% after the second dose) and two patients treated with oral anticoagulants reported local haematoma (6%) after the first dose. We didn't find the severe pain at the site of injection preventing daily activities that was present in less than 1% of participants across all age group in the phase 2/3 trial.

4.2. *Systemic reactogenicity*

Fatigue, fever (temperature $\geq 38^{\circ}$) and headache were less frequent in our patients with chronic neurological diseases (fatigue in 8%, fever in 6% and headache in 3%) than in the phase 3 trial (fatigue in 59% of younger participants and in 51% of the older ones, fever in 16% of the younger participants and 11% of the older ones and headache in respectively 52% and 39% of younger and older vaccine recipients).

Nausea and vomiting were very rare in our study (3%) as in the 2/3 phase study.

Finally, as in the phase 2/3 study, we didn't find serious adverse events related to the vaccine.

Nevertheless, we must acknowledge that our study has some limitations: the limited number of patients, the absence of a control group and the short follow-up time period (less than two months after the second dose).

5. Conclusion

The two-dose regimen of BNT162b2/Cominarty vaccine (30 μg per dose, given 28 days apart) seems to be safe in a brief follow-up period in chronic neurological patients hospitalised in our neurological rehabilitation unit. Other studies are required to detect the long-term effects of this vaccine in chronic neurological patients.

Disclosure of interest

The authors declare that they have no competing interest.

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