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Original Research

# The BNT162b2 mRNA COVID-19 vaccine in adolescents and young adults with cancer: A monocentric experience



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**Abstract** *Background and aims:* COVID-19 infection in paediatric patients with cancer is severe or critical in 20% of the patients. It can therefore directly affect paediatric patients with cancer and/or their care. We aimed at evaluating the safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine in adolescents and young adults (AYA) with solid tumour.

*Methods:* This study includes a retrospective analysis of safety and efficacy of the BNT162b2 mRNA COVID-19 vaccine administered to patients,  $\geq 16$  years old, under treatment for a solid tumour or within 6 months after treatment from 15th February 2021 to 15th April 2021. Two administrations of the vaccine 3 weeks apart were given. Sera were tested for anti-SARS-Cov-2 immunoglobulin G (IgG) antibodies directed against the S1 domain of the spike protein. In case of positive serology, neutralisation of SARS-Cov-2 was tested.

*Results:* Twenty-three patients with solid tumours were identified and proposed to get vaccinated. Nine patients refused, and 1 previously developed COVID-19 infection with positive serology. At the time of writing, 13 patients (10 M/2 F; median age: 17) started vaccination. All patients received 2 injections except 2 patients who stopped vaccination because of tumour progression. Ten patients were under treatment (alone or in combination: chemotherapy: 7 patients [pts], immunotherapy: 2 pts, targeted therapy: 3 pts, follow-up: 3 patients). Overall, vaccines were well tolerated. Five patients did not report any side-effects after the first injection and 4 after the second injection. The main local reactivity symptom was mild pain at the site of injection (6 and 2 pts). Fatigue (2 pts and 5 pts) was the most frequent systemic symptom. One

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patient refused serology testing. All patients but 1 had pre-vaccination negative serology; 7 of 10 patients tested had positive serology before second vaccine injection, and 9 of 10 patients had positive serology one month after the second injection. All patients with seroconversion had positive COVID-19 neutralisation test. No patient developed COVID infections.

**Conclusions:** We report the good safety profile and good efficacy of the BNT162B2 vaccine in AYA with solid tumours. Larger series and monitoring of the kinetics of anti-Sars-Cov-2 IgG antibodies for several months are mandatory to confirm these preliminary results and to determine long-term vaccination.

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## 1. Introduction

Since its beginning, the COVID-19 pandemic has gradually directly and indirectly affected patients with chronic disease worldwide [1]. Although children are at lower risk of developing severe form of COVID-19 [2], children treated for malignancies may be at higher risk of developing severe forms than their healthy counterparts [2–5]. The global registry of COVID-19 in childhood cancer [6] reports 20% of severe and critical forms among 1500 patients. Direct and indirect consequences of COVID-19 such as delays in diagnosis or treatment can impact outcomes of these patients [7]. For children receiving experimental therapies, data are even rarer, and physicians have been very cautious. The Innovative Therapies for Children with Cancer (ITCC) have thus reported a 60% decrease of enrolment of patients in early phase clinical trials in Europe [8].

Despite initial hope in drug repurposing, medical treatments such as chloroquine have largely failed to help clearing the virus, although the use of heparin, steroids and oxygen has greatly helped to improve outcomes of patients [9–11]. As for today, beyond social distancing, vaccines are the main tools to prevent further spread of the pandemic and protect people from the infection [12].

We report here a retrospective monocentric experience with the RNAm vaccine in adolescents and young adults (AYA) with solid malignancies under treatment or 6 months after completion of treatment treated in our department.

## 2. Patients and methods

### 2.1. Population

AYA older than 16 years old, under treatment for their malignancies or who had completed their treatment within 6 months and followed in the department of paediatric immunology, haematology and oncology, of the children hospital of La Timone, AP-HM, were proposed to receive the BNT162b2 mRNA COVID-19 vaccine.

### 2.2. Treatment

Patients were planned to receive two doses, 21 days apart, of the BNT162b2 vaccine (30 µg per dose). BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion-stabilised, membrane-anchored SARS-CoV-2 full-length spike protein [12].

### 2.3. Methods

Sera samples were tested for anti-SARS-Cov-2 immunoglobulin G (IgG) antibodies directed against the S1 domain of the spike protein of the virus using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Euroimmun®, Luebeck, Germany) as recommended by the manufacturer. All samples with an ELISA ratio  $\geq 0.7$ , neutralising antibodies against SARS-Cov-2, were detected using a virus neutralisation test (VNT100), as previously described [13]. Serial dilutions of sera 1/10 to 1/160 were tested, and specimens with a VNT100 titre  $\geq 40$  were considered positive, those with a titre at 20 indeterminate and  $< 20$ , negative. Samples were taken before first administration (T0), before second administration (T1) and one month after the second administration of the vaccine (T2).

### 2.4. Ethic

All data have been generated as part of the routine care at Assistance Publique-Hôpitaux de Marseille, and this study results from routine clinical management. The study was approved by the AP-HM, and access to the patients' biological and registry data issued from the hospital information system was approved by the data protection committee of Assistance Publique-Hôpitaux de Marseille (APHM PADS21-136). All patients signed informed consent.

## 3. Results

Twenty-three patients were identified and proposed the BNT162b2 mRNA COVID-19 vaccine. Of these 23 patients, 9 refused to receive the vaccine. The reasons

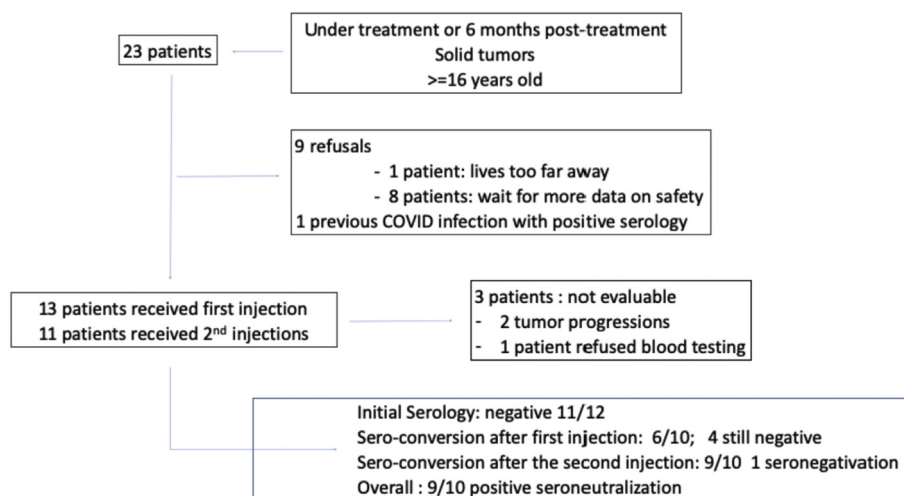


Fig. 1. Flowchart of patients.

for refusal were the fear of developing side-effect, the lack of long-term knowledge about tolerance for 8 patients and living too far from the hospital for 1 patient. One patient did not receive the vaccine as he already had developed COVID-19 [14] and still displayed positive serology and positive virus neutralisation test. Therefore, 13 patients started vaccination (see Fig. 1). The characteristics of these 13 patients are given in Table 1. Patients were receiving chemotherapy (7 patients), targeted therapies (2 patients) or immunotherapies (2 patients) alone or in combination. Three patients were in follow-up.

Two patients did not receive the second injection because of tumour progression and also lived far away from our institution. They received palliative care only.

Overall, vaccines were well tolerated. Five of 13 patients did not report any side-effects after the first injection and 4 of 11 after the second injection. The most frequent side-effect was a mild-to-moderate pain at the injection site (6 patients) that resolved within

1–2 days. The second administration seemed to be slightly less well tolerated with more frequent systemic reactions. Details of side-effects are reported in Table 2. Systemic events including fever and chills were observed within the first 1–2 days after vaccination and resolved shortly thereafter. Aside from transient local and systemic reactions, no safety concerns were identified (see Table 3).

All patients but one were negative for COVID-19 serology before immunisation. This patient did not previously develop COVID-19 symptoms, and the second serology was negative. Overall, 3 weeks after the first injection, 8 of 10 tested patients developed seroconversion, and one month after the second administration, the vaccine led to a seroconversion in 9 of 10 tested patients with positive COVID neutralisation test in all. The only patient with negative serology 1 month after the second serology had a positive serology at the time of the second injection and positive seroneutralisation. No patients developed COVID after immunisation.

Table 1  
Patient characteristics.

Patient	Age (years) (at first injection)	Gender	Diagnosis	Ongoing treatment	No of previous lines of treatment
1	21	M	B cell lymphoma	Follow-up	2
2	16	M	Low-grade glioma	Trametinib	0
3	19	F	Ewing sarcoma	Metronomic cyclophosphamide	0
4	18	M	MGT	Follow-up	2
5	17	M	Ewing sarcoma	Metronomic navelbine-cyclophosphamide	1
6	18	M	ALCL	Vinblastine	4
7	17	M	Ewing sarcoma	Metronomic cyclophosphamide	1
8	16	F	Rhabdomyosarcoma	Chemotherapy	0
9	17	M	Osteosarcoma	Durvalumab-tremelimumab	2
10	17	M	Ewing Sarcoma	Nivolumab-lirilumab	4
11	16	M	MGT	Follow-up	0
12	16	M	Desmoid tumour	Pazopanib-vinblastine	0
13	16	M	Rhabdoid tumour	Metronomic chemotherapy + bevacizumab	0

ALCL: anaplastic large-cell lymphoma, MGT: malignant germinal tumours.

Table 2  
Immunisation of patients.

Patient	T0	T1	T2	Seroneutralisation
1	Neg	Neg	Pos	Pos
2	Neg	Pos	Pos	Pos
3	Neg	Pos	Pos	Pos
4	Neg	Pos	Pos	Pos
5	Neg	Neg	Pos	ND
6	Neg	Neg	Pos	Pos
7	ND	Pos	Pos	Pos
8	Pos	Neg	Pos	Pos
9	Neg	ND	ND	ND
10	Neg	ND	ND	ND
11	ND	ND	ND	ND
12	Neg	Pos	Pos	Pos
13	Neg	Pos	Neg	Pos

ND: not done.

One patient refused serology to be performed.

One patient stopped the vaccination program after tumour progression.

#### 4. Discussion

We report here our experience with the immunisation with a COVID-19 mRNA vaccine of AYA under treatment or shortly after completion of treatment for a solid tumour. Our results show a high rate of refusal, a good tolerance and a high immunogenicity in a real-life setting of immunocompromised paediatric patients. To the best of our knowledge, our results are the first reported in AYA with cancer; it is therefore impossible to compare it with other experiences. Adverse events are consistent with those previously reported in healthy AYA [12].

Preliminary studies reported that healthy children and adolescents under the age of 15 vaccinated against sars-Cov-2 have a very high rate of protection compared with a healthy adult. In patients with cancer, only adult data are reported. Monin *et al.* [15] recently reported that in 56 adult patients with solid tumours, one dose of the BNT162b2 vaccine yielded only poor efficacy at day 21 with 38% of the patients with positive

anti-S IgG titres. However, in our study, almost all children with solid tumours seroconverted after the second dose of the vaccine.

The series we report here has some limitations. We studied a small number of patients in a single centre. Patients were limited to AYA with solid tumour and therefore do not reflect most of the paediatric oncology patients. In addition, the study was conducted over a short period up to one month after the second dose of the vaccine; it would be necessary to continue monitoring the kinetics of anti-sars-Cov-2 IgG antibodies for several months to assess vaccine protection over time.

If our preliminary results are confirmed, such a vaccine could be proposed to AYA before the initiation of their treatment and during treatment to prevent severe forms of COVID-19 or additional complications related to the disease that may compromise their oncologic treatment and in turn their long-term outcomes.

Close follow-up remains mandatory to detect rare or unknown side-effects of the vaccine in this very specific population or interactions with oncologic treatment or procedures such as radiation recall [16] or hypermetabolic lymphadenopathy by [(18)F]fluorodeoxyglucose positron-emission tomography-computed tomography [17].

Importantly, although both the American Society of Clinical Oncology and the European Society of Medical Oncology have advocated for patients with cancer a high priority status to get access to COVID-19 vaccines [18], we have observed a high rate of refusal, much higher than recently reported by Di Noia *et al.* [19] in a large Italian adult series (904 patients), in which an 11% refusal rate was observed. Elsewhere, Barriere *et al.* [20] performed a survey among adult patients with cancer in France. Among the respondents, 536 (54%) reported their intent to be vaccinated, whereas 297 (30%) considered they were not ready yet but could change their mind, and 166 (17%) patients reported to definitely refuse vaccination.

It is therefore crucial that adequate information and education is brought to paediatric patients with cancer and their family to increase enrolment in vaccination programs and in turn the success of the campaign. Education strategies must be developed with respect to AYA-specific needs and habits, for example through social media [21] or webinars [22] to make it happen as urged by Curigliano G and Eggermont [23].

#### 5. Conclusion

We report here a preliminary experience with RNA vaccines in AYA with solid tumours and report a good safety profile and excellent immunogenicity. Larger series and monitoring of the kinetics of anti-Sars-Cov-2 IgG antibodies for several months are mandatory to

Table 3  
Toxicity of vaccines.

Toxicity	First administration	Second Administration
	Number of patients (13 patients)	Number of patients (11 patients)
No toxicity	5	4
Systemic reactivity	3	5
- Fever	2	4
- Asthenia	2	5
- Vomiting	0	1
- Headaches	1	0
Local reactivity	6	2
- Pain	6	2



