

# Risk of Side Effects of COMIRNATY Intramuscular Injection for 5 to 11 Years Old in Children during the Omicron Wave in Japan

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## ABSTRACT

Efficacy of vaccination of the COMIRNATY intramuscular injection for 5 to 11 years old (Pfizer/BioNTech) against coronavirus infectious disease-2019 (COVID-19) was high in pediatric trials conducted for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants before omicron wave. Among adults, estimated vaccine effectiveness of 2 BNT162b2 (Pfizer/BioNTech) doses against symptomatic Omicron infection was reduced compared with prior variants. It has been clarified that the incidence of side effects on BNT162b2 is higher in Japanese than in other races. Therefore, we investigated the onset of side effects on the COMIRNATY intramuscular injection for 5 to 11 years old in Japanese children (5 to 11 years old) by clinical research. From the results of clinical studies, it was clarified that the incidence of side effects on the COMIRNATY intramuscular injection for 5 to 11 years old in Japanese children is extremely low. Here, we describe the symptoms of side effects on the COMIRNATY intramuscular injection for 5 to 11 years old in Japanese children.

**KEYWORDS:** COMIRNATY, COVID-19, Children, side effects

As of January 2022, more than 330 million people have been infected with SARS-CoV-2 worldwide.<sup>1</sup> In Japan, widespread vaccination of COVID-19 mRNA vaccines against SARS-CoV-2 has greatly improved the prognosis of COVID-19 among adults and elderly persons with high availability of COVID-19 mRNA vaccines and approximately 80% rates of vaccinations. In the spring of 2022, the Japanese Ministry of Health, Labour and Welfare extended mass programmes to children aged 5 to 11 years when the the COMIRNATY, an intramuscular injection mRNA based COVID-19 vaccine (Pfizer and BioNTech) was approved for emergency use in this age group. To assess the risk of acute and post-acute side effects after vaccination of COVID-19 mRNA vaccine in children aged 5 to 11 years, we conducted a prospective observational clinical study (Japan National Hospital Organization clinical Study) in children aged 5–11 years.

The number of infections by age due to omicron type SARS-CoV-2 variant (B.1.1.529; BA.1, BA.2) in children under 10 years old are high compared to delta type SARS-CoV-2 variant (B.1.617.2).<sup>2</sup> Hence, on 21<sup>st</sup> January 2022, the Japanese Ministry of Health, Labour and Welfare approved the COMIRNATY, an intramuscular injection for 5–11 years old manufactured by Pfizer and BioNTech. The first and second dose of this coronavirus disease-19 (COVID-19) mRNA vaccine was administered to children aged 5–11 years old from 15<sup>th</sup> March 2022.

In Japan, only Pfizer and BioNTech manufactures this vaccine for children aged 5–11 years, which has been approved by the Japanese Ministry of Health, Labour and Welfare. COMIRNATY intramuscular injection contains 1/3 of the amount of mRNA as COMIRNATY intramuscular injection (BNT162b2) for over 12 year olds; thus it must be used cautiously. It has been reported that COMIRNATY intramuscular injection has a 90% or higher preventive effect in 5–

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11 year olds against the onset of COVID-19. It was also discovered to have protective effect against paediatric multisystem inflammatory syndrome, which is a serious disease in children infected with SRAS-CoV-2.<sup>3,4</sup> The epidemic variant of SARS-CoV-2 evolved into an omicron type SARS-CoV-2 variant, and the paediatric COVID-19 mRNA vaccine against the omicron type SARS-CoV-2 variant showed 31% infection-prevention rate. The preventive effect of the paediatric COVID-19 mRNA vaccine against the onset of COVID-19 has also decreased to 51%.<sup>5,6</sup> Furthermore, it has been reported that the preventive effect on hospitalisation of SARS-CoV-2 infected children is 74%.

The incidence of side effects, such as myocarditis and endocarditis observed after inoculation with COMIRNATY intramuscular injection in children aged 5–11 years, was extremely low in clinical trials conducted worldwide.<sup>7</sup> The frequency of side effects observed after inoculation of COMIRNATY intramuscular injection (BNT162b2), especially serious side effects such as anaphylactic shock, is higher in Japan when compared to the results of other countries. Therefore, in a prospective observational clinical study (Japan National Hospital Organization clinical Study) in children aged 5–11 years (approximately 107,600 vaccinated children), we studied the onset of side effects after inoculation with COMIRNATY intramuscular injection. The results of this prospective observational clinical study were shared with the persons in charge at the Japanese Ministry of Health, Labour and Welfare on 7<sup>th</sup> April 2022. The Japanese Ministry of Health, Labour and Welfare's vaccination and vaccine subcommittee reported on the status of vaccination with the latest COVID-19 mRNA vaccine on 13<sup>th</sup> April 2022, and the contents were announced. In children aged 5–11 years, 6 cases (0.0028%) by medical institutions and 2 cases (0.0009%) by manufacturers were reported as suspected adverse reactions to inoculation of COVID-19 mRNA vaccine (estimated number of inoculations: 215,368). There were no significant adverse reactions or deaths reported.

A total of 21 cases (0.0098%) were reported with side effects observed after vaccination as described in the package insert of COMIRNATY intramuscular injection for 5–11 years old by 1<sup>st</sup> April 2022, including reports from medical institutions and manufacturers. A 10-year-old girl suffered from necrotising histiocytic lymphadenitis, a serious side effect, after receiving the COVID-19 mRNA vaccine. Clinical signs of myocarditis, pericarditis and viral pharyngitis were observed in a 7-year-old boy. Abnormal vasovagal reflex, vomiting and anguish

were observed as mild side effects. All children who displayed side effects have been relieved and are recovering. There are no significant concerns that could affect the COVID-19 mRNA vaccination system in Japan as of 1<sup>st</sup> April 2022.

The Japanese Ministry of Health, Labour and Welfare as well as medical institutions must pay closer attention to the side effects observed after inoculation of COMIRNATY intramuscular injection in 5–11 year olds reported in Japan and abroad. Additionally, they must evaluate and analyse the side effects observed after vaccination. Furthermore, based on the latest reports of the side effects, the Japanese Ministry of Health, Labour and Welfare must inform and alert the general population about the risks and side effects.

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### Conflict of Interest

The authors declare that they have no conflict of interest concerning this article.

### Informed Consent

Not applicable.

### Author Contributions

TH designed the research, and TH and IK collected and analyzed data. TH and IK wrote and approved the final paper.

### Data Availability

The author declares that data supporting the findings of this study are available within the article.

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