Updated report of COVID-19 vaccine safety monitoring in Japan: Booster shots and paediatric vaccinations

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International sharing of coronavirus disease 2019 (COVID-19) vaccine safety information is important for discussing the benefit-risk balance of COVID-19 vaccination at individual and population levels. We previously introduced the Japanese systems for COVID-19 vaccines safety monitoring, which represented the first and second COVID-19 vaccinations in Japan.[1] The implementation of the booster (third) shot began December 2021, and the mass vaccination of children aged 5–11 years started in February 2022. The current report is a COVID-19 vaccine safety information update for December 2021 to May 2022.

As of 15 May 2022, among a national population of approximately 125 million, there were 71,521,265 (approximately 57%) people who received the third shot of mRNA vaccines (Appendix p 1). Among 40,923,719 third shots of BNT162b2 (Pfizer-BioNTech), there were 1,585 (0·0039%) reports from healthcare professionals and 858 (0·0021%) from the marketing authorisation holder (MAH); the proportions were lower than those for the first (0·0162% [13,885/85,814,203] and 0·0135% [11,624/85,814,203], respectively) and second shots (0·0157% [13,297/84,679,372] and 0·0082% [6,937/84,679,372], respectively). Among 30,597,546 third shots of mRNA-1273 (Moderna/Takeda), there were 712 (0·0023%) reports from healthcare professionals and 420 (0.0014%) from the MAH; also lower than those for the first (0·0165% [2,705/16,397,849] and 0·0091% [1,486/16,397,849], respectively) and second shots (0·0093% [1,511/16,228,058] and 0·0064% [1,035/16,228,058], respectively). The age and sex distributions are shown in Appendix pp 2–3.

Since 6 December 2021, reporting has been mandatory for any myocarditis/pericarditis cases within 28 days after receiving a COVID-19 vaccine, for further investigation. The number of reports of myocarditis/pericarditis (any suspected cases) are shown in the Table and Appendix p 4. As of 15 May 2022, the overall reporting rates of myocarditis/pericarditis were generally lower for the third shot than those for the first and second shots, although the reporting rates of myocarditis/pericarditis among young men with third shots tended to be higher than for first shots but were lower than second shots. The number of confirmed cases of myocarditis/pericarditis (Brighton classifications 1–3) is shown in Appendix p 5. The reporting rates of anaphylaxis and thrombosis with thrombocytopenia syndrome tended to be also lower for the third shot than for the first and second shots (Appendix pp 6-7). Regarding deaths, the number of deduplicated reports from both healthcare professionals and MAH was 134 for BNT162b2 and 78 for mRNA-1273. The reported cause of death varied widely (Appendix p 8), whereas no cases were confirmed by experts suggesting a causal relationship between vaccination and death. By specific causes of death (hemorrhagic stroke, ischemic heart disease,

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		First shot				Second shot				Third shot			
		Male		Female		Male		Female		Male		Female	
Vaccine type	Age (years)	No.	No./1M shots	No.	No./1M shots	No.	No./1M shots	No.	No./1M shots	No.	No./1M shots	No.	No./1M shots
BNT162b2	12–14	6	5·6	2	2.0	44	41·6	4	4.0	2	10·1	0	0
	15–19	11	5·4	7	3·5	67	33·2	4	2.0	5	10·5	0	0
	20–24	5	3·4	3	1·8	27	18·9	0	0	1	2·3	1	1·6
	25–29	2	1·2	0	0	21	13.0	2	1·1	0	0	3	4·1
	30–34	2	1·1	3	1·4	7	4.0	1	0·5	1	1·7	1	1·3
	35–39	3	1·4	5	2.0	6	2·9	3	1·2	1	1·4	0	0
	40–44	1	0·4	4	1·4	11	4·5	1	0·4	0	0	0	0
	45–49	3	1.0	2	0·6	4	1·3	2	0·6	0	0	0	0
	50–54	2	0·6	5	1·4	5	1·6	1	0·3	2	1·5	0	0
	55–59	3	1·1	1	0·3	3	1·1	2	0·6	1	0·8	0	0
	60–64	0	0	1	0·3	2	0·7	4	1·3	0	0	1	0·6
	65–69	4	1·2	5	1·4	3	0·9	0	0	0	0	0	0
	70–74	3	0·7	6	1·3	1	0·2	4	0·9	1	0·4	2	0·7
	75–79	4	1·4	2	0·6	3	1·1	1	0·3	0	0	0	0
	80–	6	1·5	6	0·8	12	2·9	14	2.0	2	0·8	2	0·4
	unknown	12	–	7	–	5	–	4	–	0	–	0	–
mRNA-1273	12–14	1	18·5	0	0	5	103·5	0	0	0	0	0	0
	15–19	7	20·2	0	0	43	129·6	2	6·1	6	36.0	0	0
	20–24	5	4·5	0	0	67	61·4	2	2·2	12	21·3	2	3·1
	25–29	5	5.0	0	0	39	39·8	2	2·7	5	8.0	1	1·6
	30–34	2	2·1	2	3·1	11	11·6	0	0	5	7.0	0	0
	35–39	3	3.0	1	1·5	5	5.0	2	3.0	0	0	0	0
	40–44	2	2.0	0	0	4	4.0	1	1·5	0	0	0	0
	45–49	2	1·7	3	3·9	5	4·4	3	4.0	0	0	0	0
	50–54	0	0	1	1·5	2	1·9	3	4·4	0	0	0	0
	55–59	1	1·2	0	0	3	3·7	0	0	1	0·7	0	0
	60–64	0	0	0	0	1	2.0	1	3·3	0	0	0	0
	65–69	0	0	1	5·6	1	4·2	1	5·7	0	0	0	0
	70–74	0	0	1	6·6	0	0	0	0	1	0·6	0	0
	75–79	0	0	0	0	0	0	0	0	0	0	0	0
	80–	0	0	0	0	0	0	0	0	1	0·8	0	0
	unknown	4	–	1	–	4	–	2	–	1	–	0	–

***Table*: Number of individual case safety reports for myocarditis from marketing authorization holders (any suspected cases) by number of shots until 15 May 2022.**
1M: 1 million.

pulmonary embolism, ischemic stroke, myocarditis and pericarditis), the reporting rates after the third shot were lower than the background incidence rates, except for myocarditis and pericarditis (Appendix pp 9–11).

For children aged 5–11 years, as of 15 May 2022, 2,025,594 shots of BNT162b2 (Pfizer-BioNTech) were administered as the first or second shot. Among 1,146,334 first shots, there were 53 (0·0046%) reports from healthcare professionals and 50 (0·0044%) from the MAH. Among 879,260 second shots, there were 23 (0·0026%) reports from healthcare professionals and 16 (0·0018%) from the MAH. The number of reports for suspected myocarditis from the MAH was three for the first and two for the second shot, respectively, none of which were confirmed by experts with Brighton classifications 1–3. The number of suspected pericarditis cases was two and zero for the first and second shots, respectively, one of which was confirmed by experts with Brighton classifications 1–3 (0·9 cases per 1 million shots). There was one report of death after the second shot, which occurred in a patient on a ventilator for hypoxic ischemic encephalopathy with severe neonatal asphyxia at birth.

In summary, the overall reporting rate of serious adverse events associated with the third shot was generally lower than those for the first and second shots, in line with findings from the US and UK.[2-5] Several factors may explain these results, such as the long intervals between the second and third shots, and a half dose of the first/second shots was used for the booster shot of mRNA-1273 in Japan. The reporting rates for myocarditis/pericarditis in young men might have been influenced by the regulatory action implemented 6 December 2021. The reporting rate for myocarditis/pericarditis was very low in children aged 5–11 years, in line with the reports of the US and UK.[5–9] Considering these statistics, no additional safety-related regulatory actions were issued by the Japanese government from 7 December 2021 to 10 June 2022. Ongoing efforts are being made by the Japanese government to collect and present updated safety information.

Contributors

TY, MI, and CI drafted the manuscript. TY, DF, HS, TT, HU, NK, and TI had full access to and verified all the data in the study and were responsible for data acquisition, analysis, interpretation, and drafting the manuscript. NY, AO, TM, KN, SH, and ST contributed substantially to the data interpretation and drafting the manuscript. All authors had final responsibility for the decision to submit the manuscript for publication.

Data sharing statement

The data for this report are available to the public on the webpage (Japanese language only) of the Ministry of Health, Labour and Welfare of Japan (https://www.mhlw.go.jp/stf/shingi/shingi-kousei_284075.html).

Declaration of interests

AO receives grants from Eisai Co., Ltd, SHIONOGI & CO., LTD., Takeda Pharmaceutical Co, Eli Lilly Japan K. K., Chugai Pharmaceutical Co., Ltd., and Pfizer Japan Inc. All other authors declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lanwpc.2022.100600.

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