COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 26 JANUARY 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 26 January 2022 CV-ISMB Meeting

The 26 January 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:20 pm.

MEMBERS PRESENT

Dr John Tait

Dr Enver Yousuf

Dr Hilary Longhurst

Dr Maryann Heather

Dr Nick Cutfield

Professor Thomas Lumley

Dr Owen Sinclair

Professor Ralph Stewart

Dr Kyle Eggleton

Dr Tom Hills

Professor Chris Frampton

Professor Lisa Stamp

Dr Anja Werno

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Astrid Koornneef, Director, National Immunisation Programme

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

Science and Technical Advisory

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Dr Laura Young, Saskia Schuitemaker, Dr Ian Town, and Associate Professor Matt Doogue.

1.2 Minutes of the 15 December 2021 Meeting

The minutes of the 15 December 2021 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

The Chair is waiting for an update from a forensic pathologist on the pending case of concern discussed at the meeting on 8 December.

The Chair will be attending a meeting with the Acting Chief Coroner to better align efforts to detect cases with fatal outcomes where the events could potentially be linked to the vaccine and align communications to the public.

A second paediatrician has been invited to join the Board as the Programme moves to vaccinate 5–11-year-olds.

1.4 Update from the Director of the National Immunisation Programme

The Director thanked the Board for their efforts.

The Director discussed the change in scope of the programme and widening the programme to include all immunisations in New Zealand.

The Director stated that the CV-ISMB would remain focused on COVID-19 vaccinations.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Comirnaty vaccination in individuals with pre-existing heart conditions

Background

Previously, observed vs expected analyses found an increased risk of myocarditis and pericarditis.

This raised the question of whether people with pre-existing heart conditions are at greater risk of vaccine-induced symptoms, and that these possibly may go undiagnosed.

The new analysis followed subjects hospitalised prior to and post vaccination. Two survival models were used to compare the hazard between vaccinated and unvaccinated cohorts. The first hazard model was a constant hazard model. The second hazard model had temporal and age effects.

The constant hazard showed a significant reduction in the risk of death in the vaccinated cohort; however, this is not logical as there is no mechanism for the vaccine to provide protection beyond the protection it offers against COVID-19.

The adjusted hazard model showed no significant difference between the vaccinated and unvaccinated cohorts.

Discussion

The Board was asked if they had any comments about the data presented or if they require further data from the data and analytics team.

The Board considered that the data was reassuring and that these findings were consistent with that found in other countries.

The Board noted there was approximately 30,000 people, evenly split between vaccinated and unvaccinated, and approximately 2,000 events.

The Board recommended that a further analysis be conducted stratifying by severity of heart failure. However, this may not be possible from the data available, although using a proxy of such a number by hospitalisations may work.

Recommendation 1

Select Board members will continue to review the work.

2.1.2 Myocarditis and pericarditis long-term follow up study

Background

There is a study being planned to investigate the long-term outcomes in individuals diagnosed with myocarditis, pericarditis or myo-pericarditis following vaccination with Comirnaty.

A Research Oversight Committee has been set up, and feedback from the committee has been incorporated into the design of the study.

The study has been granted provisional ethics approval.

It is hoped that full ethical approval will be granted within a week.

Discussion

No comments from the Board.

2.1.3 AstraZeneca reporting to date

Background

There have been at total of 4,883 doses of the AstraZeneca vaccine administered in New Zealand.

There have been 8 serious AEFI reports, including five anaphylactic type reactions. Of the anaphylactic type reactions, four had previously had similar reactions to the Pfizer (Comirnaty) vaccine.

Common adverse effects reported in New Zealand reflect international reporting.

Serious AEFI reported in New Zealand include anaphylaxis, a known identified risk.

Health professionals and consumers should be aware of possible thrombosis with thrombocytopenia syndrome (TTS) post vaccination, a rare side effect of the AstraZeneca COVID-19 vaccine.

Discussion

The Board agreed that the use of the AstraZeneca vaccine was likely to be different than in other countries as it is being in people recommended to not get Comirnaty, and that therefore the profile of adverse events reported was therefore likely to be different.

The Board asked how the rates of reporting for people who had AstraZeneca compared to Pfizer.

The rate of reporting was higher for AstraZeneca than for Pfizer, but significantly fewer doses have been administered.

The Board inquired about reports from people who had mixed vaccine courses.

There were reports from people who had experienced an adverse event after both vaccines, including four of the AstraZeneca anaphylaxes reports.

The Board asked why several people were listed as not yet recovered.
It was explained that this was the outcome at the time the report was made.

The Board discussed the details of reports of anaphylaxis and whether they are true anaphylaxis or anaphylactoid reactions.

It was answered by Medsafe and CARM that the Brighton criteria is applied to these cases. Several cases required emergency care or hospitalisation and one case required ICU care.

The Board asked about hospitalisations.

The response was that of the patients who had anaphylaxis following AstraZeneca, two went to the emergency department, one to ICU, one was hospitalised.

The Board asked for clarification around what the criteria for labelling a report as requiring hospitalisation is.

CARM explained that the classification used is that four or more hours is recorded as hospitalised and fewer than four hours recorded as an emergency department visit.

Recommendation 2

The Board has recommended the safety of the AstraZeneca vaccine continues to be monitored through routine pharmacovigilance.

2.1.4 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome following Comirnaty

Background

There has been considerable public interest in new onset or flare ups of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) following vaccination.

It was noted that there are 57 reports of ME/CFS relapse in the CARM database following Comirnaty.

In addition, there were 9 reports of new onset ME/CFS or ME/CFS type symptoms following vaccination in the CARM database.

Using American data, an observed vs expected analysis by the sponsor showed no statistically significant change in risk.

The Associated New Zealand Myalgic Encephalomyelitis Society survey findings were presented.

It was noted that there was no literature found on the risk of ME/CFS following Comirnaty. Literature on ME/CFS following HPV Gardasil vaccination was presented. The conclusion was that there was no increased risk following vaccination.

A study following the H1N1 flu pandemic was presented, showing ME/CFS was increased by influenza infection but not by influenza vaccination.

There was similarity noted between ‘long covid’ and ME/CFS.

Overall, the conclusion was that the data did not support any increase in risk following vaccination.

Discussion

CARM commented that they have had challenges coding ME/CFS presentations, particularly self-reported new onset ME/CFS as it is unclear from the report if adequate ME/CFS criteria has been applied to the diagnosis.

The Board noted that ME/CFS patients may have a high rate of nocebo effects and that there is a high level of anxiety around relapses. Fatigue is a known side effect of the vaccine, some people with ME/CFS may have normal post-vaccination fatigue.

The Board felt reassured by the data and recommended the continuation of routine pharmacovigilance to monitor this.

The Board also discussed the diagnostic difficulties in ME/CFS and that these difficulties with diagnosis are likely to contribute to the lack of reporting in academic journals and by other regulators.

Recommendation 3

Continue to monitor through routine pharmacovigilance.

2.1.5 Update on Guillain-Barre Syndrome

Background

This is an update to a previous presentation from 2021.

Only three cases had hospital discharge summaries. All were considered to have possible causal links to vaccination.

The majority of cases reported to CARM of Guillain-Barré syndrome had a symptom onset within 24 hours.

Observational studies from the UK found an increased risk following the AstraZeneca vaccine and no increase in risk following mRNA vaccination.

There has been no significant regulatory review or action identified since the last update to the Board.

Discussion

The Board was asked for comments on individual cases, or any other questions or comments.

The Board commented that it is difficult to ascribe causality based on brief summaries. Based on the background incidence rate, New Zealand could expect around 80 cases in vaccinated individuals in a calendar year.

The Board noted that an observed versus expect analysis could be provided.

CARM stated that most rare conditions were coded as unclassifiable.

Recommendation 4

Continue to monitor through routine pharmacovigilance.

3.0 OTHER BUSINESS

3.1 CV-ISMB Annual Report

The Board received an update on their annual report for 2021 set to be published on the Ministry's website.

The Ministry of Health requested that any objections, clarifications, comments, or requests for more time be submitted.

There were no comments from the Board.

3.2 Reflection and Review Period

The Chair asked the Board to take some time to reflect and review on past CV-ISMB meetings and provide recommendations for the Ministry in how to support the CV-ISMB's work.

The Ministry left the meeting. One Ministry representative remained to take minutes.

The Committee noted that:

- The frequency of meetings and length seems to be about right.
- There have been a few different people attending meetings and it's unclear who they are; suggested that they could post name/role in meeting chat.
- Consensus that with cases presented at ad-hoc meetings, further detail is needed in advance of meeting to allow preparation.
- International evidence and the observed versus expected analysis being provided for the different safety signals investigated is helpful.
- If further expertise is needed during paediatric roll-out or in general, agreement that people will be asked to attend meetings as needed.

The Chair thanked members, the Secretariat for their attendance and closed the meeting at 5:20pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 9 FEBRUARY 2022 CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 9 February 2022 CV-ISMB Meeting

The 9 February 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:50 pm.

MEMBERS PRESENT

Dr John Tait

Dr Hilary Longhurst

Dr Nick Cutfield

Professor Thomas Lumley

Dr Owen Sinclair

Professor Ralph Stewart

Dr Tom Hills

Professor Chris Frampton

Dr Wendy Hunter

Associate Professor Matt Doogue

Dr Laura Young

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

Science and Technical Advisory

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Dr Ian Town, Professor Lisa Stamp, Saskia Schuitemaker, Dr Enver Yousuf, Dr Anja Werno, Dr Maryann Heather, and Dr Kyle Eggleton.

1.2 Minutes of the 26 January 2022 Meeting

The minutes of the 26 January 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

The Chair welcomed Dr Wendy Hunter to the Board. Dr Hunter is a paediatrician at Nelson Marlborough District Health Board.

The Chair noted that the Chair of the COVID-19 Vaccine Technical Advisory Group (CV TAG) has delegated their role as an ex-officio member of the Board to the Clinical Lead of the National Immunisation Programme.

The Chair provided an update on a meeting with the Acting Chief Coroner. It was agreed by both parties that forensic pathologists, involved in deaths of interest to the Board, can continue to be freely contacted, however coroners must be provided any written documentation submitted to the Board.

1.4 Update of the National Immunisation Programme

The Ministry confirmed that Comirnaty supply from Pfizer remains constant despite the shortening of the dose interval for boosters.

The Ministry noted that 7,000 AstraZeneca vaccine (Covishield) doses have been administered to date.

The Ministry noted that Medsafe has provisionally approved the Novavax vaccine (Nuvaxovid). A decision to use by Cabinet is pending. The Programme is expecting only minimal uptake.

The Ministry noted that the 8-week interval for 5–11-year-olds and the use of boosters in the 12-17 population are being considered by the COVID-19 Vaccine Technical Advisory Group.

The Programme's focus remains on Boosters, with the start of the Big Boost campaign.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Myocarditis and pericarditis update

Background

Myocarditis and pericarditis rates remain extremely low as expected.

Onset is mostly clustered around four days following vaccination.

Most cases are in the 20-40 years age bracket and in males following dose two in line with the international evidence.

It remains unclear if dose interval has an effect. Data was presented in two ways to the board: one by number of cases and rates for daily interval gaps. No trend was observed across this daily analysis. Second by aggregating time intervals following the intervals selected in the Ontario study, here there appeared to be a slight trend to an increase with a longer gap. However, given the low numbers of reports with dose intervals longer than 6 weeks this was not considered to be meaningful.

Discussion

The Board did not comment.

2.1.2 Myocarditis and pericarditis long-term follow up study

Background

Observational study to investigate the long-term outcomes in individuals diagnosed with myocarditis, pericarditis or myo-pericarditis following vaccination with Comirnaty.

A Research Oversight Committee has been set up, and feedback from the committee was incorporated into the design of the study. Another committee meeting will be scheduled prior to the commencement of the study.

Provisional ethics approval obtained with full approval pending.

The study is set to commence in March. Consumers will be surveyed by an independent provider, CBG Health, who have extensive experience in conducting health surveys.

Discussion

The Board did not comment.

2.1.3 Current safety information for 5-11-year-olds

Background

Current vaccine uptake shows an equity gap with Māori and Pasifika children vaccination rates falling behind children of other ethnicities.

The majority of adverse event reports are expected reactions, and mirror, what has been observed in people 12 years and older for Comirnaty.

Reports to date generally describe localised events and systemic reactions. No reports of unexpected adverse events have been received. Reporting mirrors that received following Gardasil vaccine rollout.

Most cases are classified as non-serious, with one serious report. Ten reports required emergency care, most were vasovagal reactions, and one was an anaphylactic reaction. To date, one case has required hospitalisation for observation of cardiac symptoms. Follow-up investigations did not find myocarditis and/or pericarditis.

Medication errors are occurring, including the administration of adult doses to children, however, these are being closely monitored and there is currently no evidence this is leading to adverse events.

New Zealand reporting mirrors that seen by other regulators including the Food and Drug Administration (FDA).

The main concern remains cases of myocarditis and pericarditis. The Therapeutic Goods Agency (TGA) has had 10 reports, but these did not meet the case criteria however, 1 is still under investigation.

Discussion

CARM commented that particular focus is being given to medication errors to detect any adverse events because of these.

CARM further highlighted that follow-up for any serious case is prioritised, particularly any with cardiac symptoms, as it was for the reported case of hospitalisation.

The Board thanked the Ministry for the presentation but noted concern over the inequitable rollout, which is worse than the adult rollout.

The Board noted that the lack of equitable uptake will have safety implications in vulnerable populations, putting them at risk of contracting COVID-19 infection.

The Board felt that despite the promises from the Government that this would no longer be the case, following the Waitangi Tribunal, the rates of vaccination for Māori children have been inequitable.

The Chair noted strong agreement to these comments and asked the Ministry to provide a view on the CV-ISMB's ability to release a statement regarding these comments as a Board assigned to provide safety governance.

The Ministry agreed that the CV-ISMB should provide these views and welcomed a statement. The Ministry noted that this will be provided to the Programme Director and Director-General.

The Chair asked the Board if they would like this to be highlighted as a concern from the Board; the Board supported this motion.

The Board noted that another unintended and unfortunate effect of the COVID-19 vaccine rollout is that other immunisation rates for other vaccines are falling substantially, particularly in Māori and Pasifika children, which presents a real emergency with serious equity concerns and a significant risk of an epidemic
.
The Ministry commented that the move from the COVID-19 Vaccine and Immunisation Programme to the National Immunisation Programme was done to minimise the risk of this. The Ministry's Immunisation team has been moved into the Programme to provide a unified immunisation response at the request of the Director-General.

Recommendation 1

The Board recommended the safety of the paediatric Comirnaty vaccine continues to be monitored through routine pharmacovigilance.

Recommendation 2

The Board requested a communication to the Director General and the Director, National Immunisation Programme to highlight the safety concerns around the inequities of the 5-11-year-old rollout.

2.1.4 Update on safety information of booster doses

Background

Comirnaty has provisional approval as a booster, six months following the second dose. The reduction to 3 months is considered unapproved use.

AstraZeneca vaccine is available as an alternative for the primary course of immunisation; it is not approved as a booster. Its use as a booster is unapproved use.

No unexpected serious adverse events were observed following the administration of booster doses. There was a lower reported rate for most of the adverse events than for dose one and two, with the exception of lymphadenopathy.

Other regulators report the same findings. Pfizer has confirmed there is an increased rate of lymphadenopathy following the booster dose, which was seen in the clinical trial.

AESIs continue to be closely monitored overseas and in New Zealand but no new findings have been detected.

Discussion

The Board did not comment.

Recommendation 3

The Board recommended that safety of Comirnaty booster doses continues to be monitored through routine pharmacovigilance.

3.0 CASE REPORTS

3.1 Fatal reports and other adverse event reports were presented to the Board for commentary

CARM noted that follow up is still pending for a number of cases, so in some instances current information on the report is limited. It was confirmed that these reports would be brought back to the Board when additional information had been obtained.

On review of the cases the Board noted that the adverse events described in the cases were not known side effects of Comirnaty. In addition, it was noted that in the majority of the cases significant co-morbidity and risk factors had been reported for the person involved.

The Board considered that none of the fatal cases discussed appeared to be related to the administration of the vaccine.

4.0 OTHER BUSINESS

4.1 Official Information Act (OIA) Requests

The Chair commented that there is significant public interest in CV-ISMB matters, including numerous OIA requests.

The Board was asked if they had any concerns about the publishing of their names, which are due to be released under the OIA.

The Board had no reservations.

The Chair noted that the Ministry is looking to proactively release CV-ISMB minutes for public interest. The Board was asked if they consent.

The Board felt that whatever happens to CV-ISMB minutes should mirror what happens to other expert advisory boards. The Board asked for time to review the minutes prior to release.

The Chair thanked members, the Secretariat and the Ministry staff for their attendance and closed the meeting at 5:50pm.

Dr John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 9 MARCH 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 9 March 2022 CV-ISMB Meeting

The 9 March 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:50 pm.

MEMBERS PRESENT

Dr John Tait

Dr Hilary Longhurst

Dr Maryann Heather

Saskia Schuitemaker

Dr Nick Cutfield

Professor Thomas Lumley

Dr Owen Sinclair

Professor Ralph Stewart

Dr Tom Hills

Professor Chris Frampton

Associate Professor Matt Doogue

Professor Lisa Stamp

Dr Laura Young

Dr Wendy Hunter

Dr Kyle Eggleton

Dr Enver Yousef

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Dr Anja Werno.

1.2 Minutes of the 2 March 2022 Meeting

The minutes of the 2 March 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

The Chair thanked the Board for the feedback provided on the statement circulated following the last meeting. This has been incorporated into a memo that has been sent to the Director General and Director of the National Immunisation Programme.

The Chair noted a presentation at the COVID-19 Vaccine Technical Advisory Group (CV TAG) on 8 March that provided an update on myocarditis research work, with notable presentations from Post-Event team members.

1.4 CV-ISMB Terms of Reference

The Ministry provided an update on processes and CV-ISMB Terms of Reference

The Ministry noted that the role of the Board is to provide expert advice on the safety of the vaccine, and that this includes trends or aggregated safety data, as well as individual cases where needed.

The Terms of Reference require a report at the Board's end date. The interim report for 2021 is going to Vaccine Ministers on 11 March and will be published on the Ministry of Health website.

Discussion

The Board raised a question regarding how long the Board will continue and if there are plans following the end of their tenure.

The Ministry answered that the Board will be needed at a minimum until the end of June 2022. It was noted that a memo is currently being prepared to extend the tenure of the Board until the end of June 2022. The Ministry noted further detail about how the programme will continue after June 2022 is still being decided.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Vaccine portfolio update

Background

The Novavax (Nuvaxovid) vaccine can be booked from 9 March, with first doses available as early as 11 March. This will follow a two-dose regime (3 weeks apart) for those 18 years or older.

To this date the Pfizer vaccine remains the primary vaccine used by the Programme.

Noted discussions at CV TAG regarding a booster for 12-17-year-olds. Advice has been provided to be signed out soon.

The 8-week interval remains current advice for 5–11-year-olds, rationale provided around both immunogenicity and side effects.

Noted Janssen provisional approval granted however initial supply issues.

Moderna still going through approval process.

Discussion

The Board asked about the pathway for 16–17-year-olds who do not want another Pfizer dose.

The Ministry responded that off-label prescribing has been used in other situations. There is currently no approval for use of other COVID-19 vaccines in children.

The Board noted that this issue has been raised by the exemption group and work with CV TAG is ongoing.

The Board asked about the dose interval recommendation for children and what safety data supports this.

Comment from the Board that from an immunological perspective anywhere between a 3 and 8 week interval should be fine.

Comment that CV TAG have been presented with a reasonable amount of evidence to support the 8-week interval.

2.1.2 Update on myocarditis

Background

Observed versus expected analysis using the National Minimum Dataset (NMDS), following people after vaccination for 21 days (risk window). Compared against background rates from the SAFE study.

The New Zealand data is largely following international trends of younger adult age groups more at risk for myocarditis and pericarditis after the Pfizer vaccine.

The 12–19 age group produced a high relative risk, largely attributable to the background rate data range being for 0-19 years which is not representative. Currently trying to control for this using self-controlled case series.

The Ministry also provided an update on the long-term follow up study of reported cases of myocarditis and pericarditis

Short-term international data available for people who have developed myocarditis indicates it is generally mild and self-limiting, however there is no long-term data.

The Centres for Disease Control & Prevention (CDC) are doing similar work and have published some provisional results for 12-29-year-olds which is reassuring. It was found that after a minimum of 90 days following diagnosis, most people did not report a significant impact on quality of life.

The New Zealand study is observational in the form of a survey to the consumer and their healthcare provider. Conducted primarily via a phone survey delivered by registered nurses. Participants will be identified by a report to CARM. The healthcare record will be utilised to support information gathering.

Ethics approval received, estimate 300 eligible participants. Study expected to commence by the end of March with results in June.

Discussion

The Board commented that relative risk presented relates to diagnosis and reporting myocarditis and pericarditis, not the relative risk of having developed the myocarditis and pericarditis.

Question from the Board around whether we need to start looking at the long-term central nervous system effects of the vaccine.

Noted by the Board that there is an interesting study recently from the UK about COVID-19 causing brain injury. They did large scale MRI for this which is not trivial and would require a large amount of resource and standardisation. Comment that imaging based studies and psychometric based studies would be difficult. It will be interesting to see how this evolves internationally and if it is replicated in any other studies.

Question from the Board about looking into long-term effects of the vaccine versus potential long-term effects of COVID-19 infection and the harm avoided with vaccination.

Answered by the Ministry that the main aim will be to look at the safety of the vaccine. It was agreed that this also needs to be looked at in the context of harm from COVID-19 infection.

2.1.3 Qlik Overview

Background

Reporting by ethnicity shows that most reports are being received by European and other, with low levels of reporting for Pacific Peoples.

Preferred term reported by ethnicity shows the frequency of events is similar. Most common are headache, dizziness, injection site pain and lethargy.

Most frequently reported preferred term in the paediatric age group are dizziness, nausea, vomiting, pallor and headache.

Discussion

The Board did not comment.

2.1.4 Underreporting for Pacific Peoples

Background

Reporting rate for Pacific Peoples is currently 2.4 AFEI per 1,000 vaccinations, significantly lower than other ethnic groups. Overall reporting rate for COVID-19 vaccines is ~5.5 AEFI per 1,000 vaccinations.

Identified a need to increase reporting in Pacific Peoples to ensure their experience is captured and to ensure safety data is reflective of the New Zealand population.

Key area in attempt to leverage this data is utilizing existing engagement channels.

The Programme is working closely with Ministry of Health, Pacific Health and Communications teams to produce simplified and accessible messaging around the who, what, when, where and how for AEFI reporting.

Current radio campaign run by Cause Collective (Pacific Social Change Agency) about COVID-19 and Omicron has included key messages on reporting. Key messaging also shared with Ministry of Pacific Peoples and Ministry of Social Development to share with their stakeholders.

Discussion

The Board commented that the general principle around why people are not engaging with the health system more broadly is important.

The Board commented that this is potentially a system issue rather than a person not engaging and it is good to see attempts to try and address some of these access issues.

Comment emphasizing the use of community leaders is important. This includes the healthcare profession (i.e., GPs) and how this profession is also key in information sharing.

2.1.5 Memo - People with persisting disability after Comirnaty

Background

'Persisting disability' does not have a universal definition, outside of pharmacovigilance it has quite a strict definition in some contexts.

Due to the way the data is collected, it is not always clear from the report the symptoms which have persisted.

It was identified some unexpected symptoms of serious reports were reported symptoms of long COVID (loss of smell/taste).

Persisting disability has not been noted as a concern by other regulators, although individual conditions that can take time to recover have been (e.g., myocarditis).

Discussion

CARM noted that during the course of monitoring the case definition changed. Agreed that persistent disability traditionally is used in the definition presented (e.g., causes

significant impact). Question raised whether we should be looking more closely at reports with persisting symptoms (that do not truly meet definition of persisting disability). Noted that many of the non-specific cases occur as a collection of symptoms.

The Board noted that symptoms do not necessarily mean persisting disability and felt broadly reassured by the data. Medically unexplained symptoms are always very challenging. Those suffering will often attribute their experience to infections, medicines, vaccines and foods etc.

Comment that if people have ongoing symptoms, they should be seen for assessment rather than simply attributing them to the vaccine.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Fatal Cases

CARM presented an update on recently reported fatal cases.

3.2 Other cases

CARM provided an overview on other recent reports of interest since the last meeting.

4.0 OTHER BUSINESS

4.1 No other business

The Chair thanked members, the Secretariat and the Ministry staff for their attendance and closed the meeting at 5:50pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 30 MARCH 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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MINUTES OF 30 March 2022 CV-ISMB Meeting

The 30 March 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:33 pm.

MEMBERS PRESENT

Dr John Tait

Dr Enver Yousuf

Dr Hilary Longhurst,

Dr Anja Werno,

Dr Maryann Heather,

Saskia Schuitemaker,

Dr Nick Cutfield,

Professor Matt Doogue,

Professor Thomas Lumley,

Dr Owen Sinclair,

Professor Ralph Stewart,

Dr Tom Hills,

Professor Lisa Stamp,

Dr Laura Young,

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Professor Chris Frampton, Dr Kyle Eggleton and Dr Wendy Hunter.

1.2 Minutes of the 9 March 2022 Meeting

The minutes of the 9 March 2022 meeting were accepted as a true and accurate record of the meeting.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Post Vaccine Symptom Check (PVSC)

Background

The Ministry provided an overview of the design and progress of PVSC.

The booster campaign is ongoing and scheduled to end on 1 April 2022.

The paediatric PVSC campaign is ongoing.

Key inclusion criteria are a New Zealand mobile number, no previous adverse event following immunisation (AEFI) reported to CARM in order to ensure this is purely active monitoring, and oversampling of Māori and Pacific peoples.

There have been a low number of participants invited for the paediatric campaign as parents are contacted, therefore this requires the ability to adequately link parent and child COVID Immunisation Register (CIR) profiles and obtain contact information.

Key findings from PVSC include that booster doses in adults are not more reactogenic than dose one or dose two, only 18% of surveyed children experienced side effects which is approximately half the adult rate, and Pacific people are most likely to visit a GP in the days soon after vaccination.

Discussion

The Board asked if there was any analysis that interrogated if following the increased awareness of myocarditis as a rare side effect of vaccination, if there was a resulting increase in the reporting of cardiac symptoms.

The Ministry noted that a campaign was started to increase myocarditis awareness. A text search of the PVSC booster data for terms used to raise awareness of myocarditis (e.g., fluttering) after the campaign started, found no increase in reporting of cardiac symptoms.

The Board noted that the JAMA meta-analysis on the nocebo effect in the placebo arms of the Pfizer clinical trials should be considered when interpreting the PVSC data.

2.1.2 Myocarditis

Background

Medsafe provided an update on myocarditis.

There was discussion around current reports of myocarditis in certain age brackets. Myocarditis reports were most common for males aged 20-40 years old. There were no cases in children under 10 with a clinical diagnosis.

The analysis on a difference in incidence depending on the dose interval is still inconclusive.

Discussion

The Board asked if people who have myocarditis or pericarditis after dose one or two go on to have subsequent doses.

It was answered that some have had a second dose of Comirnaty don't report side effects; some have had the AstraZeneca vaccine instead; many have not gone on to have other vaccinations although the Ministry is now looking to understand if this group will book in to have Nuvaxovid.

The Board noted that people are advised to defer subsequent doses and these people are provided with a medical exemption. Therefore, many people who developed myocarditis or pericarditis did not go on to have further vaccinations.

The Board commented that the rate of idiopathic myocarditis is the same as the rate following vaccination, with the highest incidence in males in their 20s.

Medsafe acknowledged this and noted that vaccination may be enhancing an existing biological mechanism.

2.1.3 Safety Evaluation

Background

The Ministry provided an overview of active surveillance monitoring systems.

Electronic health records are being monitored as a means of detecting signals.

The National Minimum Dataset (NMDS), the mortality database, the maternity database and the CIR, are the databases used.

An application, that compares hospital admissions since the start of the vaccination roll-out, to those prior to the vaccination roll-out is under development.

A live demonstration of the application was provided.

Discussion

The Board noted this was an elegant approach. It was asked how false positives will be managed and it was questioned how this will be implemented with different vaccines and future variants.

The Ministry replied that it is top of mind for the programme to adapt the system for influenza vaccines. It was also added that additional work is underway to prevent type 1 errors.

The Board congratulated the Ministry on the application. It was asked how the expected rate was calculated for events that did not typically result in hospitalisation.

The Ministry replied that this uses data from the background rates study (SAFE study) which uses hospitalisation (NMDS) data, and this was a known limitation. Further work is ongoing to obtain primary care background data.

The Board asked whether there was the possibility that using NMDS data for relatively mild conditions could lead to false reassurance as access to hospital services may have been restricted during the pandemic and borderline admissions may not have been admitted.

The Ministry acknowledged this and will explore how to examine this.

The Board suggested that this could be accounted for by evaluating changes in admission rates for other causes.

2.1.4 Vaccination During Pregnancy

Background

Medsafe provided an update on the safety of vaccination during pregnancy.

Despite the Comirnaty vaccine being recommended for pregnant women in dozens of countries, there is a general anxiety amongst the public about safety in pregnancy.

It was noted that the absolute rate of reporting is unknown, because there is no record of how many pregnant women there are in New Zealand at any given time.

International literature has consistently shown no increased risk of spontaneous abortion using hospital data.

The Centres for Disease Control and Prevention (CDC) released a report on pregnancy registry data for 46,000 births and 10,000 vaccinations and found no association.

Some literature has focused on outcomes for live births and found an association between vaccination and jaundice in infants, the authors attributed this increase to possible confounding due to high smoking rates in the vaccinated group. Importantly the numbers in the study were too small to draw conclusions from and this was noted in the paper.

Discussion

The Board noted that they felt reassured by the data.

Recommendation 1

The Board recommended that the safety of the Comirnaty vaccine in pregnancy continues to be monitored through routine pharmacovigilance

2.1.5 Comirnaty and Thyroid Conditions

Background

Medsafe presented a memo on thyroid conditions and Comirnaty

It was noted that there are numerous thyroid disorders, but Graves' disease and thyroiditis, are the only inflammatory conditions and therefore have plausible mechanisms of action.

There was no signal reported in the latest Pfizer Monthly Safety Monitoring Report

There is no current signal, no consistent onset time, no consistent diagnosis. Importantly, thyroid disease is relatively common so coincidental events can be expected.

Discussion

The Board commented that the data presented was reassuring. It was noted that the thyroid conditions discussed are readily managed.

Recommendation 2

The Board recommended that the safety of the Comirnaty vaccine and reports of thyroid conditions continue to be monitored through routine pharmacovigilance.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Fatal cases

CARM introduced a new format of the CV-ISMB death report and thanked the Programme for support in putting it together.

CARM presented an update on recently reported fatal cases since the last meeting.

A case was presented to the Board, where the reporting clinicians highlighted the person had symptoms that had occurred prior to the vaccination event.

Discussion

It was noted by a member of the Board that prior analysis of individuals with heart conditions, shows no increased risk of death following vaccination, and instead shows a decreased risk of death.

The Board noted that the influenza vaccine also lowers the risk of death in heart patients.

The Ministry commented that if an individual with cardiac symptoms presented to a vaccination clinic, the clinical lead in the vaccination centre is expected to triage the patient appropriately, particularly if someone presented with acute symptoms. Cardiac symptoms would take priority over the vaccine, and the patient would be sent to the emergency department.

There were no further comments on other cases presented.

3.2 Other Cases

CARM presented an update on other cases of interest since the last meeting.

There was discussion around the recovery period for these cases.

4.0 OTHER BUSINESS

4.1 No other business

The Chair thanked CARM, and the Board for their attendance and closed the meeting 5:33pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 4 MAY 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 4 May 2022 CV-ISMB Meeting

The 4 May 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 4:55 pm.

MEMBERS PRESENT

Dr John Tait

Dr Enver Yousuf

Dr Maryann Heather

Saskia Schuitemaker

Professor Thomas Lumley

Dr Nick Cutfield

Dr Kyle Eggleton

Dr Wendy Hunter

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Dr Juliet Rumball-Smith, Dr Laura Young, Dr Hilary Longhurst, Dr Anja Werno, Dr Owen Sinclair, Professor Lisa Stamp, Professor Ralph Stewart, Dr Tom Hills and, Associate Professor Matt Doogue

1.2 Minutes of the 30 March 2022 Meeting

The minutes of the 30 March 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

Third primary dose for immunocompromised 5–11-year-olds was agreed to by CV-TAG and is planned to be implemented early May.

A fourth dose (second booster) is still under discussion.

The Board's interim report for 2021 is published on the Ministry website.

Noted that there have been some comments/questions from CV TAG about interim report for the Board and/or Medsafe to respond to.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Myocarditis and pericarditis long-term follow up study

Background

The Ministry provided an update on how the study is tracking.

Commenced 30 March 2022.

It was noted there has been good engagement from consumers.

To date, 126 consumer surveys completed (78% response). Healthcare provider, 10 surveys completed out of 105 sent out (10% response rate).

Currently working internally with the communications team on strategies to increase engagement from healthcare providers.

Discussion

The Board commented that it can be challenging to engage GPs with surveys, and low response rates are usual (10%, 15% or 20%). Potentially engaging with practice managers rather than GP's, could increase responses.

Suggestion from the Board that communication through the College of GPs and content in NZ Doctor publication/newsletter could be explored.

2.1.2 Paediatric Comirnaty

Background

Medsafe provided an update on the memo presented in February 2022.

Highlighted that there are differences in uptake across ethnicities, with higher rates of vaccination in European and Asian children.

Vaccine uptake slowed significantly after the first month of the rollout (~372,000 doses; 55% first dose and 24% fully vaccinated).

Up to 3 May 2022, 780 AEFI reports – 619 for dose one and 161 for dose two.

The rate of reporting is lower after dose two and the overall reporting is lower in the 5–11-year-olds than in those 12 years and older. Similar trends have been observed in other countries (i.e., Australia).

Dizziness and nausea are the most frequently reported symptoms, with reporting rates similar across doses.

Majority of reports are non-serious, with a small number of cases requiring emergency care or hospitalisation (including chest pain and anaphylaxis). No confirmed cases of myocarditis and/or pericarditis.

Post Vaccine Symptom Check (PVSC) data for 5–11-year-olds recently published on Medsafe website; 79% of people did not report a reaction, similar symptoms reported to what is reported to CARM.

VigiLyze has 5,859 reports for 5–11-year-olds. The most frequently reported symptoms are pyrexia, headache, vaccination site pain, and vomiting.

Reporting in New Zealand is consistent with the international experience.

Discussion

The Chair commented that the numbers in rollout are still disappointing. Questioned whether there had been any change in reporting after the death of the teenager was notified.

Medsafe noted that there had not been noticeable increase in reporting.

The Board commented that circulating COVID could have affected vaccination numbers due to the recommended three-month gap following infection. It was noted that there have been high infection levels in the younger age group.

2.1.3 COVID-19 booster vaccines update and safety of booster in under 18's

Background

Medsafe provided an update on the safety data for boosters in New Zealand and international data for boosters in 16 and 17-year-olds.

Three vaccines available as a booster in New Zealand.

Comirnaty is the preferred and only regulator-approved booster vaccine. Noted that AstraZeneca and Nuvaxovid currently unapproved by Medsafe as a booster.

Majority of the reports are from members of the public. Headache and injection site pain most common reported symptoms along with other reactogenic reactions.

There have been some cases of myocarditis and pericarditis reported following a booster dose of Comirnaty but no indication that these events are more frequent or severe.

No new overall safety concerns identified. Majority of reports internationally and in New Zealand are expected reactogenic events.

Discussion
There were no comments from the Board.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Fatal cases

The Director of the New Zealand Pharmacovigilance Centre provided an overview of recent fatal reports received by CARM.

Comment that the number of serious reports and death reports has declined in recent months.

3.2 Other Cases

The Director of the New Zealand Pharmacovigilance Centre provided an update on other recent reports received by CARM.

4.0 OTHER BUSINESS

4.1 No other business

The Chair thanked CARM, and the Board for their attendance and closed the meeting at 4:55 pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 18 MAY 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 18 May 2022 CV-ISMB Meeting

The 18 May 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 4:32 pm.

MEMBERS PRESENT

Dr Hilary Longhurst (Deputy Chair)

Dr Enver Yousuf

Dr Maryann Heather

Saskia Schuitemaker

Professor Thomas Lumley

Dr Nick Cutfield

Dr Wendy Hunter

Dr Tom Hills

Dr Laura Young

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Post-Event, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

Group Manager, Clinical, National Immunisation Programme

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The chair welcomed the attendees to the meeting. Apologies were received from Dr Anja Werno, Dr Owen Sinclair, Professor Lisa Stamp, Professor Ralph Stewart, Associate Professor Matt Doogue, Dr John Tait, Dr Kyle Eggleton and, Professor Chris Frampton

1.2 Minutes of the 4 May 2022 Meeting

The minutes of the 4 May 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

Discussions are still ongoing about the fourth dose (2nd booster) regarding population eligibility and rollout dates.

Currently seeking clarification on the future of the Board. A question was raised around reporting lines to the Director, National Immunisation Programme.

The Ministry commented that a memo would go from Director of the National Immunisation Programme to the Director-General of Health and Interim Lead of the National Public Health Service around reporting lines for the Board and seeking to extend tenure.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Tinnitus and hearing loss

Background

The Ministry provided an update on tinnitus and hearing loss with the COVID-19 vaccines.

A memo on tinnitus with the Pfizer COVID-19 vaccine was presented to the Board last year in August.

The scope of this memo is expanded to include hearing loss and all three COVID-19 vaccines available in New Zealand.

Tinnitus is a known side effect for the Janssen COVID-19 vaccine.

In New Zealand up to 2 May 2022, for the Pfizer COVID-19 vaccine there have been 822 reported cases of tinnitus in 779 individuals, for the AstraZeneca vaccine 11 cases in 10 individuals and the Novavax vaccine, 3 cases in 3 individuals.

Reports of hearing loss have only been received in New Zealand for the Pfizer COVID-19 vaccine; 138 reported cases in 135 individuals.

Review of the available literature was inconclusive

International regulators have not found any evidence of tinnitus or hearing loss for the Pfizer, AstraZeneca, or Novavax COVID-19 vaccines.

Review by Pfizer for tinnitus and deafness/hearing loss did not confirm a signal or causal association.

VigiLyze has more than 43,000 reports of tinnitus for the COVID-19 vaccines (>22,000 for Pfizer COVID-19 vaccine).

Uppsala Monitoring Centre performed a review of hearing loss in May 2021 with no signal confirmed.

There is currently insufficient information to confirm a signal for any of the three COVID-19 vaccines available in New Zealand.

Discussion

Chair commented that the onset time in the Swedish study referenced was very short. Question about onset time in New Zealand.

Ministry answered that the onset of symptoms for reported cases in New Zealand was within 7 days.

Board commented that there is a hint of a possible association, however the current evidence is not definitive. Agree with current recommendation to continue monitoring with routine pharmacovigilance.

The Board noted that data on persistence of symptoms is missing. Question as to whether it would be possible to collect this.

The Ministry noted that the information we have is only from what is reported to CARM and would need further follow-up.

Chair asked for a comment from CARM.

The Director of the New Zealand Pharmacovigilance Centre noted that the only information available is what is reported and followed up shortly after. In order to obtain further detail would need a study.

The Board commented that the balance of the international data is very reassuring.

Recommendation 1:

The Board recommends continuing to monitor through routine pharmacovigilance

2.1.2 Nuvaxovid post-marketing safety data

Background

Medsafe provided an update on the post-marketing safety data for the Novavax vaccine.

Limited data to date, due to limited use.

Australia is the only country, generating any reports (>100,000 doses administered).

Up to 4 May 2022, there have been 42 AEFI reports in New Zealand

An observed versus expected analysis (O/E) conducted by the Sponsor indicates a potential signal for myocarditis although not published in the safety report.

No data available from literature.

Propose to closely monitor reports of myocarditis/pericarditis cases.

Discussion

Question from the Board if the Sponsor's O/E is based on the spontaneous reports and whether Australia was driving available data.

Medsafe answered that O/E was from spontaneous data and ~90% of post-market data is from Australia.

Recommendation 1:

The Board that Medsafe should wait until Australia finishes their analysis for myocarditis/pericarditis with the Novavax vaccine and then make a call on whether local action is needed.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Fatal Cases

The Director of the New Zealand Pharmacovigilance Centre provided an overview of recent fatal reports received by CARM.

3.2 Other cases

There was an update from the New Zealand Pharmacovigilance Centre on other recent reports received by CARM.

Discussion

There were no comments from the Board.

4.0 OTHER BUSINESS

4.1 No Other Business

The Chair thanked CARM, and the Board for their attendance and closed the meeting at 4:32 pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 22 JUNE 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 22 June 2022 CV-ISMB Meeting

The 22 June 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:40 pm.

MEMBERS PRESENT

Dr John Tait

Dr Enver Yousuf

Dr Maryann Heather

Saskia Schuitemaker

Professor Thomas Lumley

Professor Ralph Stewart

Dr Kyle Eggleton

Associate Professor Matt Doogue

Dr Nick Cutfield

Dr Laura Young

Dr Hilary Longhurst

Dr Anja Werno

Professor Lisa Stamp

Dr Tom Hills

Dr Owen Sinclair

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Vaccine Safety Surveillance and Research, National Immunisation Programme (NIP)

Director, New Zealand Pharmacovigilance Centre

Group Manager National Contracts, Quality and Workforce, National Immunisation Programme

Research & Insights Lead, Communications and Engagement, National Immunisation Programme

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The chair welcomed the attendees to the meeting. Apologies were received by Dr Wendy Hunter, Professor Chris Frampton and Dr Juliet Rumball-Smith.

1.2 Minutes of the 18 May 2022 Meeting

The minutes of the 18 May 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

The Chair noted that fourth dose (second booster) has gone through parliament, with vaccinations likely to start in July; however, the final decision on the eligible groups is yet to be announced, groups likely to include Māori and Pacific Peoples aged 50 and older, and 65 and older for the rest of the population.

The Chair noted that the National Immunisation Programme is transitioning to Health New Zealand from the first of July 2022.

It was also noted that the CV-ISMB tenure has been extended until September 2022, however there are questions as to whether this should be extended to the end of December 2022 to align with the COVID-19 Vaccine Technical Advisory Group (CV TAG).

It was confirmed by the Group Manager, Vaccine Safety Surveillance and Research that a memo is currently being drafted to propose extending CV-ISMB tenure to align with CV TAG tenure.

There was discussion regarding the significance of the Board's expertise and its continued importance to the National Immunisation Programme.

The Chair suggested that a discussion is had with the Director of the National Immunisation Programme about the future of the Board.

2.0 NATIONAL IMMUNISATION PROGRAMME MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Myocarditis and pericarditis education

Background

The National Immunisation Programme provided a summary of myocarditis and pericarditis awareness and education in New Zealand.

A survey invitation was sent out to vaccinators and site leads at most recognised vaccination sites (GP, pharmacies, dedicated vaccination sites).

The survey received a good response rate of 1300 vaccinators and site leads.

Some key findings from the survey were explained:

- Around 10% of respondents who were involved in the consent process, indicated that they were aware of myocarditis and pericarditis as a possible risk associated with the vaccine but did not use this information in the consent process.
- Explanations given on why verbal information on myocarditis and pericarditis was sometimes, rarely, or never given included:
    - Not wanting to worry people or put people off getting vaccinated.
    - Feeling time pressure, i.e., to vaccinate as many people as possible in the time available.
    - Some consumers were not interested in hearing information and just wanted to get their vaccination over with.
    - Some vaccinators indicated that they only discussed the risk with those they perceived to be most at risk.
- Explanations given on why brochures on myocarditis and pericarditis information were sometimes, rarely or never given included:
    - Brochures were not available or up to date with latest information
    - Some consumers were not interested or didn't want a physical brochure
    - Some vaccinators only gave physical brochures out after the first dose (and after not subsequent doses)
    - Vaccinators indicated they thought verbal consent was enough

It was noted that a summary report is being prepared to consolidate feedback and actions to address the issues identified.

Discussion

A member of the Board asked if there was a difference in results based on provider type (e.g., pharmacy versus dedicated vaccination sites).

It was answered that although this was not the primary aim of the survey, there did not appear to be a difference based on provider type.

The member suggested it may be helpful for this results breakdown to include Māori and Pacific health providers as distinct groups.

The Programme acknowledged the exemplary work performed as part of the COVID-19 vaccination rollout, and that most learnings from the survey centre around how we can more effectively share information with and prepare the vaccinating workforce.

2.1.2 Consumer Experience

Background

The National Immunisation Programme provided a summary of the results of research on the vaccine experience from the consumer's perspective.

This data was collected via an online survey, with a link included in an email invite from The Ministry of Health. The invitation list consisted of people who had been vaccinated in the previous two weeks, and 6 waves of the study have been conducted.

Net Promotor Score (NPS) was used as the key metric for the study to measure how the consumers felt about their experience (complimented by other satisfaction metrics). A high NPS score indicates a positive consumer experience.

Overall, the results were positive, with a high proportion of participants recommending/being satisfied with the experience. It was noted that only a small proportion of participants expressed a negative sentiment towards the vaccine experience.

This study had sufficient participation numbers across all equity groups including Māori, Pasifika, and disabled peoples, and showed a consistent trend across all these groups.

This study also asked participants for improvements that they believed could be made for a more positive experience during vaccination. The most frequently reported areas for improvement were:

- A more supportive and accommodating environment for children.
- (Continue to) be professional, helpful, and friendly.
- Provide the right information (more/better/consistent).
- Provide more information on long term side effects.
- Reduce wait times and maintain good hygiene practices at vaccination centres.

Discussion

There was discussion from the Board around this item

3.0 PHARMACOVIGILANCE MATTERS

3.1.1 AEFI Overview/Update

Background

Medsafe provided an overview/update of adverse events following immunisation (AEFI) reporting to date.

It was noted that the Comirnaty vaccine remains the most commonly used COVID-19 vaccine in New Zealand.

With regards to rates of AEFI reporting, it was noted that:

- The highest rate of AEFI reporting is after dose one; the reporting rate is lower after dose two, and lower still after dose three.
- There are very low numbers of AEFI reports for the AstraZeneca and Nuvaxovid vaccines.
- The demographic distribution of reports remains unchanged, with the lowest reporting rate seen in Pacific Peoples. It was noted that this is unlikely to change significantly given most people have now been vaccinated.

- The reporting rate is observed to be the lowest for children, and highest for those in the 25-40-year age group.
- Females have a higher reporting rate of AEFIs compared to males.

Several other observations were made, including that:

- The most commonly reported AEFIs remain unchanged from previous updates.
- The highest reporting group is members of the public (via webform), followed by vaccinators and nurses.
- There has been an increase in reporting from GPs using the BPAC e-reporting module.

It was noted that there have been many reports of myocarditis/pericarditis but only approximately half appear to have had a clinical diagnosis; this could in part be due to the nocebo effect and stimulated reporting due to awareness, which could impact both consumers and healthcare providers.

Discussion

The Board noted that the overall picture is similar to past reporting.

There were no further comments or questions.

3.1.2 Vaccine effectiveness

Background

The Ministry provided a summary of international literature on vaccine effectiveness (VE). It was noted that analysis of New Zealand data is still underway.

It was noted that clinical trial data shows promising efficacy. It was identified clinical trials do not take into account real world issues like repeated exposure to a vaccine, waning immunity, or comorbidities.

Limitations to VE studies can include the context at the time, such as the dominant variant, the makeup of vaccine coverage, time since vaccination, and the specific outcomes assessed by the study. A recent study on VE conducted in Qatar during an Omicron outbreak was described as an example.

It was noted that there is evidence to suggest that immunity from vaccination wanes over time, however many studies only assess VE at a specific timepoint.

A meta-regression analysis of 21 studies showed waning of VE at 6 months for hospitalisation in all ages (10%), and significantly more waning for infection or symptomatic infection (20-30%).

Several papers indicated that boosters restore waning immunity and increase VE against the delta variant, and that having received the primary series and a booster dose does decrease the chance of severe COVID infection.

It was also noted that evidence is emerging with regards to heterologous versus homologous vaccine schedules, however that this is possibly less relevant to New Zealand's current context where 96% vaccine coverage is with Comirnaty as a primarily homologous vaccine schedule. However, there is some heterologous use with the AstraZeneca and Nuvaxovid vaccines.

A systematic review showed that homologous mRNA schedules are the most effective but only slightly more than a heterologous mRNA booster schedule.

Discussion

There were no comments or questions from the Board.

3.1.3 Myocarditis after COVID-19 Infection

Background

The Ministry presented a memo on the international literature of myocarditis and pericarditis after infection compared with COVID-19 vaccination.

The key finding was that the risk of myocarditis and pericarditis was higher after COVID-19 infection compared to vaccination across all age groups and genders.

Overall younger males were found to be at greatest risk of myocarditis and pericarditis, but the disparity between infection and vaccination was greater in females.

Studies suggested that individuals with vaccine-related myocarditis or pericarditis had milder symptoms and better clinical outcomes.

It was also suggested that people with myocarditis or pericarditis due to COVID-19 infection were less likely to present with typical symptoms, which could make it more difficult to identify and diagnose.

The Ministry also provided an update on an exploratory analysis currently being conducted to understand what would be feasible with the New Zealand data.

Discussion

There were no questions or comments from the Board.

3.1.4 Myocarditis study update

Background

The Ministry provided a status update on the Myocarditis follow up study.

It was explained that the study has now been extended to include those with a myocarditis or pericarditis diagnosis after a third or subsequent dose of the Pfizer vaccine, and the study period has expanded to include cases occurring up to and including 28 February 2022.

Additionally, a paper survey option for healthcare providers (HCP) will now be provided to those who have not completed the online survey, as this may provide more flexibility and could be a preferred method for some HCPs.

A summary of preliminary results for overall health, mental health, physical functioning, and school and work were described from the first 150 completed consumer surveys. It was noted that results may change as data collection continues.

It was noted that participating individuals had a similar demographic distribution compared to the overall reported cases of myocarditis and pericarditis that CARM has received, in terms of age, gender and ethnicity.

Discussion

A member of the Board notes that some of the symptoms experienced over long time periods sound similar to long COVID. They questioned if objective outcome measures matched patient reported measures.

It was answered that the HCP data has not yet been analysed, but that this would be looked at.

4.0 CASE REPORTS OF SPECIAL INTEREST

4.1 Fatal Cases

CARM provided an overview of recent fatal reports.

It was noted that there were no concerning or unusual deaths, and none of the reported deaths were considered related to the vaccine. Some deaths are still under investigation due to minimal information in the original report.

4.2 Other Cases

CARM provided an update of other recent reports of interest.

5.0 OTHER BUSINESS

5.1 No other business

The Chair thanked members, the Secretariat and the Ministry staff for their attendance and closed the meeting at 5:40pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 03 AUGUST 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 3 August 2022 CV-ISMB Meeting

The 3 August 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 5:17 pm.

MEMBERS PRESENT

Dr John Tait (Chair)

Dr Enver Yousuf

Dr Hilary Longhurst

Dr Anja Werno

Dr Maryann Heather

Saskia Schuitemaker

Dr Nick Cutfield

Professor Thomas Lumley

Dr Owen Sinclair

Professor Ralph Stewart

Dr Tom Hills

Dr Laura Young

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Vaccine Safety Surveillance and Research Group, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

Acting Director, National Immunisation Programme

Data and Analytics Team, National Immunisation Programme

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received by Professor Lisa Stamp, Professor Chris Frampton, Dr Kyle Eggleton, and Associate Professor Matt Doogue

1.2 Minutes of the 22 June 2022 Meeting

The minutes of the 22 June 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

The Chair confirmed with the Director of the National Immunisation Programme that the tenure of the Board is needed until the end of the year. This decision was informed by the possibility of variant specific vaccines, vaccines for young children, and the ongoing booster campaign.

The Director has indicated that work is ongoing about whether there will be an immunisation technical advisory group (I-TAG) or broader medicines policy group.

The Board now reports to the National Director of the new National Public Health Service (NPHS) within Te Whatu Ora – Health New Zealand.

The National Director also wishes for the Board to continue until December, although meeting less frequently than every three weeks.

Vaxzevria, the AstraZeneca vaccine, is to be phased out of use in New Zealand. The last day it can be administered is 04 September 2022.

The Board thanked the Chair for the update.

1.4 Update from the National Immunisation Programme

The Acting Director of the National Immunisation Programme provided an update on the programme and the new structure within the National Public Health System (NPHS).

Work is agreed until the end of the calendar year, but not beyond that. The Public Health Agency is currently undertaking work on an immunisation strategy, where information on a new I-TAG is being drafted. There is a significant amount of parallel work going on between agencies and stability is required for the transition. Therefore, the CV-ISMB is being asked to stay until December 2022.

Second boosters are now on offer to healthcare workers aged 30 or above, and anyone aged 50 or above.

In terms of numbers, 340,000 second boosters have been administered, with nearly 63,000 of these administered in the last 7 days. This shows good uptake in the last week.

In terms of paediatrics, there was an increase in uptake over school holidays, with nearly 13,000 paediatric doses administered.

Variant specific vaccines, and vaccines for children under 5 years are on the horizon, but there is no timeline yet.

A wider area of focus for the programme is influenza. This year, Pharmac widened access to the influenza vaccine for Māori and Pacific peoples who are 55-64 years of age, children aged 3 to 12 years and people with disabilities. The programme is using tools developed for the COVID-19 immunisation campaign for the promotion of the influenza vaccine, such as SMS and emails. There has been reasonable uptake using these tools.

Another key area is childhood immunisations, where uptake has not been as good. There was a 20% equity gap in quarter four. An important area of focus is the MMR vaccine, both for initial childhood doses and the catch-up campaign.

A National Immunisation Taskforce is being established that will be chaired by Dr Owen Sinclair.

Discussion

A member of the Board asked why the age for second boosters is set at 30 years and older for health and disability workers.

Another member of the Board responded that it took a long time to come to this decision. The vaccine we have now is good for preventing serious disease but not omicron infection.

A member of the Board asked what the rationale is for not allowing people under 30 to have boosters.

The member of the Board replied that young people are allowed to have a second booster, but it is not officially recommended. Long-term efficacy against covid infection with new variants is less than for the original strain but still provides good protection against serious disease

Te Whatu Ora stated that this is about benefit versus risk. The age of 30 years was chosen due to the higher risk of myocarditis after vaccination and lower risk of severe covid infection in this age group. In addition, 30 years is only for health and aged care workers due to increased risk of exposure. It is 50 years for other groups. Ultimately, this is an individual risk benefit decision that must be made by a person with their health care provider.

A member of the Board noted that the language around ‘recommended’ versus ‘available for’ versus ‘not yet needed’ can be confusing.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry of Health and Te Whatu Ora

2.1.1 Vaccine Efficacy in New Zealand Context

Background

Te Whatu Ora-Health New Zealand gave a presentation on vaccine efficacy using New Zealand data.

The purpose of this work was to identify people most at risk of infection and understand herd immunity in New Zealand.

Te Whatu Ora noted that the data was observational rather than experimental which meant there were limitations to consider. For example, they were reliant on individuals testing and reporting symptomatic infection. Behaviour around testing and reporting varies via vaccination status meaning they could not do a comparison study between vaccinated and unvaccinated cohorts.

The efficacy of the vaccine wanes over time and there is a linear increase in infection rate as time increases following a booster dose. The longer the time interval after the booster, the higher the infection rates in that population.

Infection induced immunity also shows waning, the month following infection has the highest protection, about 95%, which declines significantly within 6 months to around 80%.

For efficacy against severe disease/hospitalisation they were able to compare groups by vaccination status as all groups still go to hospital.

At first glance, the hospitalisation rate is not too different. However, those who are older and most at risk are more likely to get their booster shots.

The adjusted likelihood shows boosted individuals have the lowest likelihood of being hospitalised. The fully vaccinated (two dose) cohort are about twice as likely (2.2) to be hospitalised as boosted people are. Those who have only had a first dose are about 4.3 times as likely compared to those boosted.

There were some problems with data in the unvaccinated cohort, for example a person who interacted with the health system in 2019 and then left the country would be counted as unvaccinated and not hospitalised.

Survival analysis estimates a 70% efficacy which decays over time. There were some challenges with time variant risk, for example people boosted before the omicron outbreak versus during. Te Whatu Ora will update the model. They anticipate the adjusted model will show much lower waning.

Discussion

CARM asked for clarification on the strain of COVID-19 circulating at the time of data collection and whether hospitalisation data was for people hospitalised due to or with COVID-19.

Te Whatu Ora responded that within the hospitalisation data they have ruled out any cases where the primary diagnosis was not COVID-19. Going back to March, it was probably the BA.2 strain. This does vary a bit over time.

2.1.2 Cases Referred to the Coroner

Background

Te Whatu Ora provided an update on three vaccine-mediated myocarditis deaths referred to the coroner.

2.1.3 Update from Medsafe

Background

Medsafe continues to get changes to the provisionally approved COVID-19 vaccines. Finalising application for AstraZeneca to be approved as a booster.

Nuvaxovid, the Novavax vaccine has made an application for primary vaccination in adolescents. Australia has added pericarditis to Nuvaxovid in their data sheet. Medsafe are investigating whether that needs to be added to product information in New Zealand and whether the company are updating their data sheet.

Anticipating an application for Comirnaty for children under 5 and an application for Comirnaty for booster doses for children aged 5-12 years old.

Medsafe is looking into how companies will submit applications for variant vaccines. There is some clinical data for earlier variants, but the Northern Hemisphere wants a BA.4 and BA.5 variant vaccine.

Discussion

A member of the Board commented that there has always been a question as to whether boosters targeting a different, newer variant might boost the original immune response (against the antigen from original variant that was in the original vaccine, which will share many antigenic epitopes with the new vaccine), rather than broadening the immune response to effectively neutralise the new variant/target (sometimes called 'original antigenic sin'). A recent research letter in NEJM, shows you can use a variant-specific protein vaccine to effectively boost against a new variant in people who had originally been vaccinated with BNT162b2. A small study, one vaccine technology, and early days, but it might indicate that 'original antigenic sin' will not be too much of a problem.

The member of the Board provided a link to the publication.

A member of the Board asked how many people have had Nuvaxovid worldwide.

Medsafe replied that there has been good uptake in Australia, about 160,000 doses administered, but uptake everywhere else was low. Medsafe will ensure their datasheet is kept up to date.

Member noted that Novavax was used in several countries including Germany, but the pericarditis link was only seen in Australia.

A member of the Board asked if there was any appetite for approaching companies for randomised introduction of vaccines and noted that when New Zealand introduces new vaccines we could do in a way where we compare effectiveness.

Medsafe replied that this is a Programme issue.

A member of the Board agreed that it would be good to know the effectiveness of each vaccine from a controlled study.

The Board stated that appetite for this would be higher scientifically than commercially.

2.1.4 Presentation on potential safety signal - vasculitis

Background

Te Whatu Ora/Medsafe investigated vasculitis as a potential safety signal.

Reports received by CARM for a condition referred to as ‘COVID toes,’ similar to what is seen after infection itself.

There are some difficulties in using hospitalisation data as many cases are handled in primary care.

Analysis of New Zealand data identified a safety signal in the 20-39 age group after dose one only. The analysis identified no other signals in any other age group after any dose.

Lareb, in the Netherlands, has also observed a possible safety signal.

Pfizer did their own study and found rates of vasculitis after vaccination did not exceed expected rates.

A review of the literature showed most publications were of case reports.

Te Whatu Ora asked the Board for their thoughts around the observed increase in risk in vasculitis in one age group.

Discussion

CARM responded that the numbers are small, and it should be noted that the medical assessors see reports come in as vasculitis and sometimes the report is clear but sometimes reports come in of vasculitis and when they follow up, they find no confirmation of vasculitis. It is often another condition.

A member of the Board commented that the aetiology of vasculitis is often unclear. Often, people will look for a temporal relationship with a vaccine. Noted the very small numbers. The member supported continuing to monitor but did not feel that there was a safety signal.

A member of the Board agreed stating the potential safety signal did not look real. Noted that when clinicians see this type of vasculitis, they consider infection, cancer, and medications. Comment that from the data presented this seems like very small excess incidence. No evidence of a safety signal here.

A member of the Board commented in writing that that it is always difficult with coding data and D69.0 is the code for allergic purpura, which is sometimes used synonymously with urticarial vasculitis (a cutaneous vasculitis which is more common in younger people and women). But given the term is not widely used clinically, it's possible that episodes of acute urticaria (caused by any number of things including allergy) are sometimes coded as 'allergic purpura', either because it was difficult to tell if there were purpuric features clinically, or because the coding is incorrect. It might also be possible that people are more likely to seek healthcare, or be referred to hospital, for skin rashes after their first dose of a vaccine.

Recommendation 1

The Chair recommended that Medsafe should continue to observe vasculitis, but the Board does not believe there is a safety signal.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Deaths and Case Reports of Special Interest

CARM provided an update on cases.

CARM stated that the numbers of new reports are decreasing. CARM continues to investigate and follow up reports.

4.0 OTHER BUSINESS

4.1 No other business

The Chair thanked members, the Secretariat and Te Whatu Ora for their attendance and closed the meeting at 5:17pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 21 SEPTEMBER 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 21 September 2022 CV-ISMB Meeting

The 21 September 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 4:48 pm.

MEMBERS PRESENT

Dr Hilary Longhurst (Chair)

Dr Enver Yousuf

Dr Maryann Heather

Saskia Schuitemaker

Professor Ralph Stewart

Dr Laura Young

Dr Tom Hills

Dr Owen Sinclair

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Vaccine Safety Surveillance and Research, National Immunisation Programme

New Zealand Pharmacovigilance Centre

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The Chair welcomed the attendees to the meeting. Apologies were received from Dr John Tait, Professor Michael Tatley, Dr Wendy Hunter, Dr Anja Werno, Dr Nick Cutfield, Professor Lisa Stamp, Professor Thomas Lumley, Dr Kyle Eggleton, Professor Chris Frampton and, Associate Professor Matt Doogue.

1.2 Minutes of the 3 August 2022 Meeting

The minutes of the 3 August 2022 meeting were accepted as a true and accurate record of the meeting.

1.3 Update from the Chair

Medsafe have issued an Alert communication for Nuvaxovid and the risk of myocarditis and pericarditis.

The National Director, National Public Health Service is being regularly updated on Board's work; thank you to the Board for their ongoing work.

Update on recent Coroner's Inquest

- Coroner has publicly released cause of death, accepting pathologist's finding that this was a vaccine induced myocarditis.
- The inquiry is still ongoing with the coroner investigating the circumstances of the death, whether death could have been prevented and if any recommendations or comments are required.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry of Health and Te Whatu Ora

2.1.1 Nuvaxovid Update

Background

Medsafe provided an update on Nuvaxovid and the potential risk of myocarditis and pericarditis.

An alert communication was issued on 8 September 2022. This was based on the Sponsor determining a possible causal link with the vaccine and myocarditis/pericarditis.

Medsafe want to ensure healthcare professionals and vaccinators are aware of risk and counsel people to seek medical attention if they experience any symptoms.

The Data sheet for Nuvaxovid has been updated to include a warning about myocarditis and pericarditis.

Most reports of myocarditis/pericarditis received by the company have been from Australia. Demographic data of the reports shows an even split between males and females, with the highest number of reports in the male 12–17-year age range.

An observed versus expected (O/E) analysis by the company (up to the end of August), showed a significantly higher number of cases for all risk windows; statistical significance was lost when looking only at medically confirmed cases.

Other regulators have also conducted a review

- The **European Medicines Agency** (EMA) recommended that a warning be added to product label
- The **Food and Drug Association** (FDA) reviewed prior to authorisation and US product label includes a warning
- The **Therapeutic Goods Administration (**TGA) listed pericarditis as an adverse event, however, does not include a warning in the product label.

Discussion

The Board asked if the estimated rates are similar to the Pfizer and Moderna vaccines.

Medsafe answered that the FDA had thought the rates could be higher, but currently as usage is limited and number of cases is small, unable to make a meaningful comparison

2.1.2 Thrombocytopenia memo

Background

Te Whatu Ora/Medsafe investigated thrombocytopenia as a potential safety signal with the Pfizer COVID-19 vaccine

There have been 38 cases reported to CARM.

Demographic data shows, 79% of the reported cases were European, 13% Māori and 8% Asian. 58% of cases were female with the majority in people 65 years and older.

An observed versus expected (O/E) analysis of local data showed a statistically significant increase following the second dose overall and in the 60–79-year age group; the rate increase was noted to be low but still present.

When evaluating this data, need to consider limitations of the study: expected rates are based on background rates of all age groups (including under 5 years), any events occurring in primary care are not included in the observed rates and the available background rates (2014-2019) which are prior to the pandemic.

The sponsor conducted an O/E analysis using spontaneous reports which has limitations, primarily underreporting. No new safety signal identified based on review of cases and O/E analysis.

There have been case reports of thrombocytopenia published in literature, however large population-based studies show no statistically significant association between thrombocytopenia and the Pfizer vaccine.

International regulators have not recognised thrombocytopenia as a safety signal.

Insufficient information to confirm thrombocytopenia as a safety signal, recommendation is to continue monitoring through normal pharmacovigilance activities

Discussion

The Board commented that an overall analysis was more important than an age-related analysis. Comment that this was something to be looked at, however evidence was not strong for a link between event and vaccine.

Noted by the Board that the coding for thrombocytopenia can include a large number of unrelated issues e.g., infection, chemotherapy-related thrombocytopenia. Idiopathic thrombocytopenia, that can occur after vaccines is much less common and this wouldn't be expected to be more common in older age groups. Comment that overall, the data is reassuring.

The Board further commented that they are comfortable with the recommendation; to continue to monitor. Noting that it was good that the limitations of the analysis were outlined and need to remain cognisant of this. Comment that this could be either a chance finding or the way that we are defining our background rates. **Recommendation 1**

The Chair summed up the discussion, agreeing that monitoring should continue, and the Board have noted possible association but not clear evidence of causality.

2.1.3 Acute Kidney Injury memo

Background

Te Whatu Ora/Medsafe investigated acute kidney injury (AKI) as a potential safety signal with the Pfizer COVID-19 vaccine

This follows on from a previous presentation to the Board in August 2021 of glomerulonephritis and nephrotic syndrome. At this time, the Board agreed that routine monitoring should continue.

An O/E analysis of local data showed an increased incidence rate ratio (IRR) for AKI in those 20 years and older for dose one and all ages in dose two.

The limitations of the data were noted: specificity the ICD-10 codes (unspecified kidney injury contributed significantly to the elevated IRR results), clinical record assessments were not conducted (unclear what 'unspecified kidney injury' covers) and sex/ethnicity/comorbidities were not adjusted for.

Sponsor and the European Medicines Agency investigated glomerulonephritis and nephrotic syndrome with no link established and the recommendation was to continue monitoring.

The available literature for AKI following vaccination is limited. A study by Luo et al. looked at the number of AKI cases reported to VAERS; more than 1000 cases with greater than 600 possibly linked to vaccine. The authors noted many cases had confounders and risk factors for AKI such as advanced age, diabetes and chronic kidney disease.

There have been 30 cases reported to CARM, most cases had contributing risk factors and comorbidities.

There have been AKI cases reported following vaccination and COVID-19 infection. Most local cases and those reported in the literature had risk factors for developing AKI. Recommendation is to continue monitoring through normal pharmacovigilance activities.

Discussion

No comments from the Board

Recommendation 2

The Chair accepted the recommendation to continue to monitor acute kidney injury through routine pharmacovigilance activities.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Fatal Cases

Background

CARM provided an update on fatal cases

Patterns of recent reports are very similar to what has previously been presented to the Board.

3.2 Other Cases

Background

CARM presented an update on other cases of interest since the last meeting.

4.0 OTHER BUSINESS

4.1 No Other Business

The Chair thanked members, the Secretariat and Te Whatu Ora for their attendance and closed the meeting at 4:48 pm.

Dr. John Tait

Chair, CV-ISMB

COVID-19 VACCINE INDEPENDENT SAFETY MONITORING BOARD (CV-ISMB)

MINISTRY OF HEALTH, WELLINGTON

NEW ZEALAND

MINUTES OF THE 7 DECEMBER 2022

CV-ISMB MEETING

NATIONAL IMMUNISATION PROGRAMME

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Minutes of 7 December 2022 CV-ISMB Meeting

The December 2022 meeting of the CV-ISMB was held at the Ministry of Health and on Microsoft Teams. The meeting commenced at 4:00 pm and closed at 4:51 pm.

MEMBERS PRESENT

Dr John Tait (Chair)

Dr Hilary Longhurst

Dr Enver Yousuf

Dr Maryann Heather

Professor Ralph Stewart

Associate Professor Matt Doogue

Dr Laura Young

Dr Tom Hills

Dr Owen Sinclair

Dr Nick Cutfield

Professor Lisa Stamp

INVITED GUESTS AND EXPERTS IN ATTENDANCE

Medsafe, Clinical-Risk Management

Vaccine Safety Surveillance and Research Group, National Immunisation Programme

Director, New Zealand Pharmacovigilance Centre

Chief Medical Officer, Niue Department of Health

1.0 MATTERS OF ADMINISTRATION

1.1 Welcome and Apologies

The chair welcomed the attendees to the meeting. Apologies were received by Saskia Schuitemaker, Professor Thomas Lumley, Dr Kyle Eggleton, Professor Chris Frampton, Dr Wendy Hunter, and Dr Anja Werno.

2.0 PHARMACOVIGILANCE MATTERS

2.1 Matters Referred to the CV-ISMB by the Ministry

2.1.1 Memo – Bell's palsy

Background

Mesdafe provided an update on the risk of Bell's Palsy after the Comirnaty vaccination.

There have been 228 cases of Bell's Palsy reported to the Centre for Adverse Reactions Monitoring (CARM) up to 29 September 2022.

The New Zealand data sheet for Comirnaty lists 'acute peripheral facial paralysis' as a rare adverse reaction.

The international product information also lists acute facial paralysis as an adverse reaction.

The latest summary report from the Sponsor found no new significant safety information and ongoing monitoring and safety surveillance will continue.

An observed versus expected (O/E) analysis of local data was carried out and showed no statistically significant increase in risk after dose one or two of Comirnaty. A limitation is that only hospitalisation data was available to use.

A literature review found most studies conducted were case control or self-control case series studies. Most studies conclude that there is a small risk or association, or that there is no association with Bell's palsy and the Comirnaty vaccine.

Facial paralysis is a known adverse reaction of Comirnaty and there is a plausible biological mechanism for the development of this following vaccination and from COVID-19 infection. From the information presented there are no changes in safety with Comirnaty in relation to Bell's palsy and Medsafe should continue routine monitoring.

Discussion

The Board queried whether the relative risk of vaccination and infection were compared for Bell's palsy.

Medsafe answered that relative risk of vaccination and infection was not part of this investigation.

The Board asked for clarity around the definition of hospitalisation.

It was confirmed that hospitalisation referred to patients who have spent four or more hours in the emergency department.

The Board noted that most Bell's palsy cases would be handled in primary care, and in future an alternative data source could provide further insight.

The Board commented that currently there is no national database for GP data.

Recommendation 1

The Board supported Medsafe's recommendation to continue monitoring Bell's palsy through routine pharmacovigilance activities.

2.1.2 Herpes zoster

Background

Medsafe provided an update for Herpes zoster following Comirnaty vaccination. This topic was previously presented to the Board in December 2021.

CARM have received 409 reports of herpes zoster up to 28 September 2022.

An O/E analysis of local data did not show any increased risk of herpes zoster after the first three doses of Comirnaty. A limiting factor of the analysis is that using hospitalisation data only accounts for a small proportion of the herpes zoster cases in New Zealand. However, these results indicate that there is no evidence of increased risk of serious cases of herpes zoster requiring hospitalisation in New Zealand after COVD-19 vaccination.

The Sponsor has also conducted their own O/E analysis, and similarly to the New Zealand analysis, did not find any indications of a safety signal.

A review of available literature indicated overall that cases of herpes zoster following vaccination tended to be non-serious. The absolute risk of herpes zoster was very low.

The benefits of vaccination significantly outweigh the risk of herpes zoster after COVID-19 infection.

Further studies are needed to understand herpes zoster following vaccination and continued monitoring is recommended.

Discussion

The Board stated the New Zealand data is reassuring and that no regulatory action is necessary. It was noted that the majority of herpes zoster cases are handled by primary care.

The Board referenced a large study that has been published after the literature review was conducted. This study included 2 million individuals from the US claims database, as well as inpatient and outpatient visits, and showed no increased risk of herpes zoster after COVID 19 vaccinations including Comirnaty and other vaccines (Idara Akpandak, et al).

The Board indicated that herpes zoster is a sufficiently common event that the randomised control trial data may be able to define the risk without needing to use case control studies.

Recommendation 2

The Board recommended that Medsafe continue to monitor through routine pharmacovigilance.

2.1.3 Niue report

The Chief Medical Officer for the Niue Department of Health was in attendance to discuss COVID-19 vaccine safety data with the Board.

2.1.4 National Public Health Service Vote of Thanks

The National Director for the National Public Health Service thanked the Board for allowing him to attend. He thanked the Board for the work they have done in the last two years since they were established. He remarked upon the fact that the Board met frequently, considered challenging cases, and met at short notice.

The Chair thanked the National Director for attending.

The Interim Director Prevention echoed the National Directors comments and thanked the Board for the value they brought. She stated that the important work done by the Board has provided confidence out to the sector.

3.0 CASE REPORTS OF SPECIAL INTEREST

3.1 Deaths and case reports of special interest

CARM provided an update on reported deaths.

CARM noted that new cases since the last meeting show nothing unusual.

All completed cases have sufficient supplementary information relating to the case required to make necessary decisions around outcomes.

CARM noted that many fatal reports received are made without or before the cause of death is known and are therefore coded with the term sudden death. When further information is provided this can change

The Chair acknowledged the work that CARM has done over the last two years, and the contributions made to the Board.

4.0 OTHER BUSINESS

4.1 Any other business

A final report for 2022 will be prepared and circulated for to the members of the Board for review.

The National Immunisation Programme (the Programme) thanked the Board for their work. The chair has been invited to remain as chair of the Board next year. Moving forward, this Board will not meet on an ordinary basis, meetings will be on ad hoc basis for fatal cases that need CV-ISMB consideration.

The Chair stated that setting up a technical advisory group has been discussed, however there have been conversations around the Board remaining solely focused on COVID-19, while keeping in mind that there needs to be work around where all responsibilities lie.

The Board stated that a NITAG group in New Zealand would be beneficial, as New Zealand currently does not have one. Also identifying that New Zealand currently has Pharmac which uniquely affects how a NITAG would be established.

The Chair thanked members, the Secretariat and the Ministry staff for their attendance and closed the meeting at 4:51pm.

Dr. John Tait

Chair, CV-ISMB