



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Covid-19 vaccines safety surveillance

PCWP/HCPWP joint meeting – 1 June 2021

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An agency of the European Union



PhV Plan of the EU Regulatory Network for COVID-19 Vaccines

A range of measures have been put in place:

- ✓ Enhancing monitoring activities based on **H1N1** experience
- ✓ Using **new tools and methods** developed to support rapid detection and evaluation – including creation of focussed group for vaccine's monitoring
- **Reducing timeframe** for COVID-19 related signals
- **Additional transparency** measures (e.g. COVID19 monthly updates, ARs etc.)
- Establishing an **unprecedented and intense international collaboration** with **MHRA, FDA, WHO, NITAGs** and **ICMRA- PhV network** to share knowledge, experience and communications



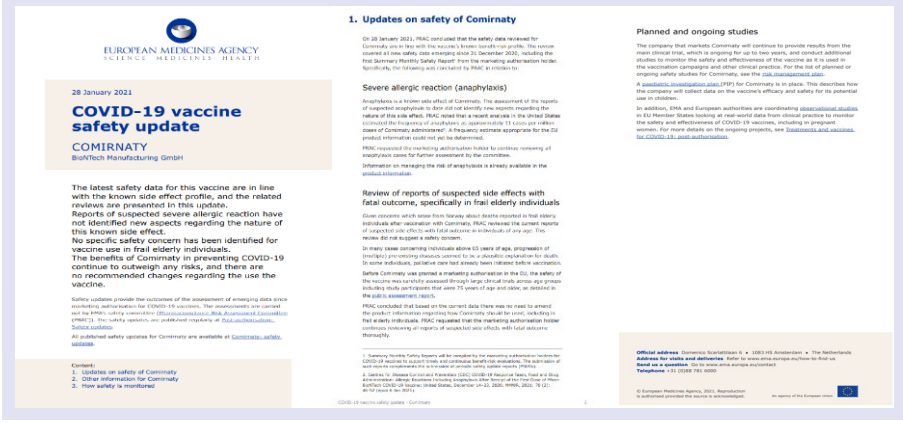
Reduced time-frame for procedures

- Summary of **Monthly Safety Reports (SMSR)**:
 - *cumulative EEA reports stratified by age, special groups, pregnancy country, etc.*
 - *Ongoing and closed signals in the interval*
 - *RMP safety concerns including O/E analyses , fatal reports etc,*
 - *Risk/benefit considerations*
 - *Etc.*

- **Rapid** signal outcomes and implementation (e.g. urgent confirmation of signals, fast update of PI etc.)
- **Extraordinary** PRAC/CHMP meeting

Risk Communication

- **EMA** Press Conference
 - Ad-hoc
 - Routine
- **Covid-19** safety updates: 16 since January
 - *Monthly aligned with SMSR and ad-hoc when needed*
 - *Timely transparency*
 - *Meaningful communication to the public, journalists and specialist stakeholders*



28 January 2021
COVID-19 vaccine safety update
COMIRNATY
 BioNTech Manufacturing GmbH

The latest safety data for this vaccine are in line with the known side effect profile, and the related reviews are presented in this update. Reports of suspected severe allergic reactions have not identified new aspects regarding the nature of this known side effect. No specific safety concerns have been identified for vaccine use in frail elderly individuals. The benefits of Comirnaty in preventing COVID-19 continue to outweigh any risks, and there are no recommended changes regarding the use of the vaccine.

1. Updates on safety of Comirnaty

Severe allergic reaction (anaphylaxis)

As mentioned in a recent safety update for Comirnaty, the assessment of the reports of suspected anaphylaxis in frail did not identify new aspects regarding the nature of this side effect. EMA will continue to monitor the safety of Comirnaty in frail elderly individuals. A frequency estimate appropriate for the full product information could not yet be determined.

EMA continued the ongoing activities related to further monitoring of anaphylaxis cases for further assessment by the committee.

Determination on managing the risk of anaphylaxis is actively available in the product information.

Review of reports of suspected side effects with fatal outcome, specifically in frail elderly individuals

Given concerns which arose from heavily about deaths resulting in frail elderly individuals after vaccination with Comirnaty, EMA reviewed the current reports of reports to the EMA with fatal outcome in individuals of any age. This review did not trigger safety concern.

In many cases concerning individuals above 65 years of age, progression of underlying pre-existing chronic disease led to a secondary indication for death. In some individuals, evidence does not entirely seem to be related before vaccination.

Given Comirnaty was prepared a preliminary publication in the EU, the safety of the vaccine was largely assessed through large clinical trials across age groups including frail participants that were 75 years of age and older, as detailed in the [EMA public assessment report](#).

EMA concluded that based on the current data there was no need to amend the public information regarding how Comirnaty can be used, including in frail elderly individuals. EMA requested that the reporting authorities keep continuously monitoring all reports of suspected side effects with fatal outcome.

Planned and ongoing studies

The company that markets Comirnaty will continue to provide results from the main clinical trial, which is ongoing till up to five years, and conduct additional studies to monitor the safety and effectiveness of the vaccine as it is used in the vaccination campaigns and other clinical practice. For the list of planned or ongoing safety studies for Comirnaty, see the [EMA public assessment report](#).

A scientific consultation (SC) report for Comirnaty is in place. This document from the company will detail data on the vaccine's efficacy and safety for its potential use in children.

In addition, EMA and European authorities are coordinating [additional studies](#) in EU Member States looking at real-world data from clinical practice to monitor the safety and effectiveness of COVID-19 vaccines, including in pregnant women. For more details on the ongoing projects, see [EMA public assessment report for COVID-19 vaccine information](#).

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Up to date overview of COVID-19 vaccines data by brand name

WW

#CASES

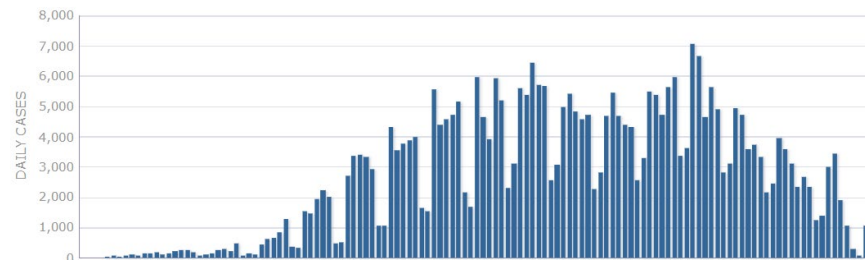
502,478

Serious	158,457
Non serious	179,596



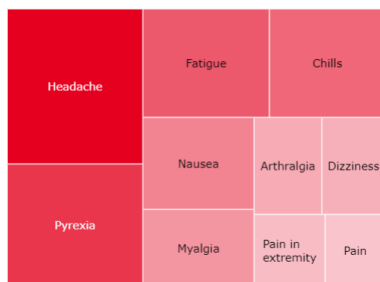
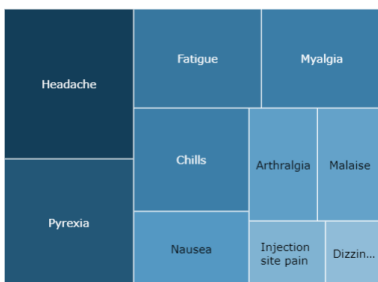
EEA

Healthcare Professional	151,526
Non HCP	186,527



RECEIVE DATE (individual counts are displayed when hovering over the bars)

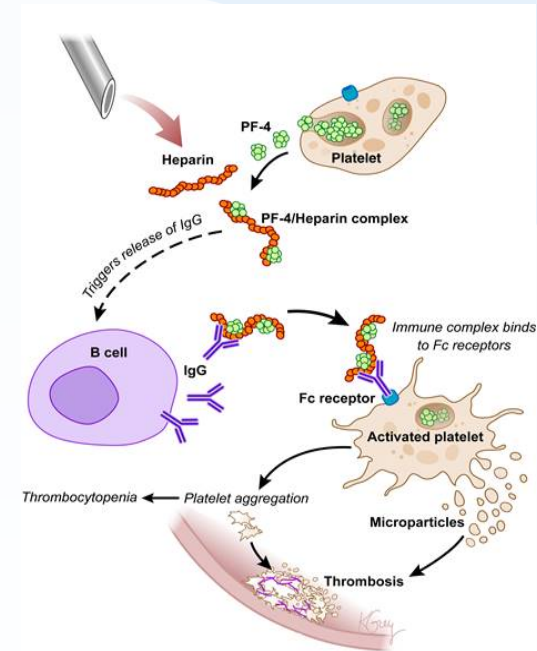
Reactions - 10 most reported PTs overall (left), in serious cases (centre), and in fatal cases



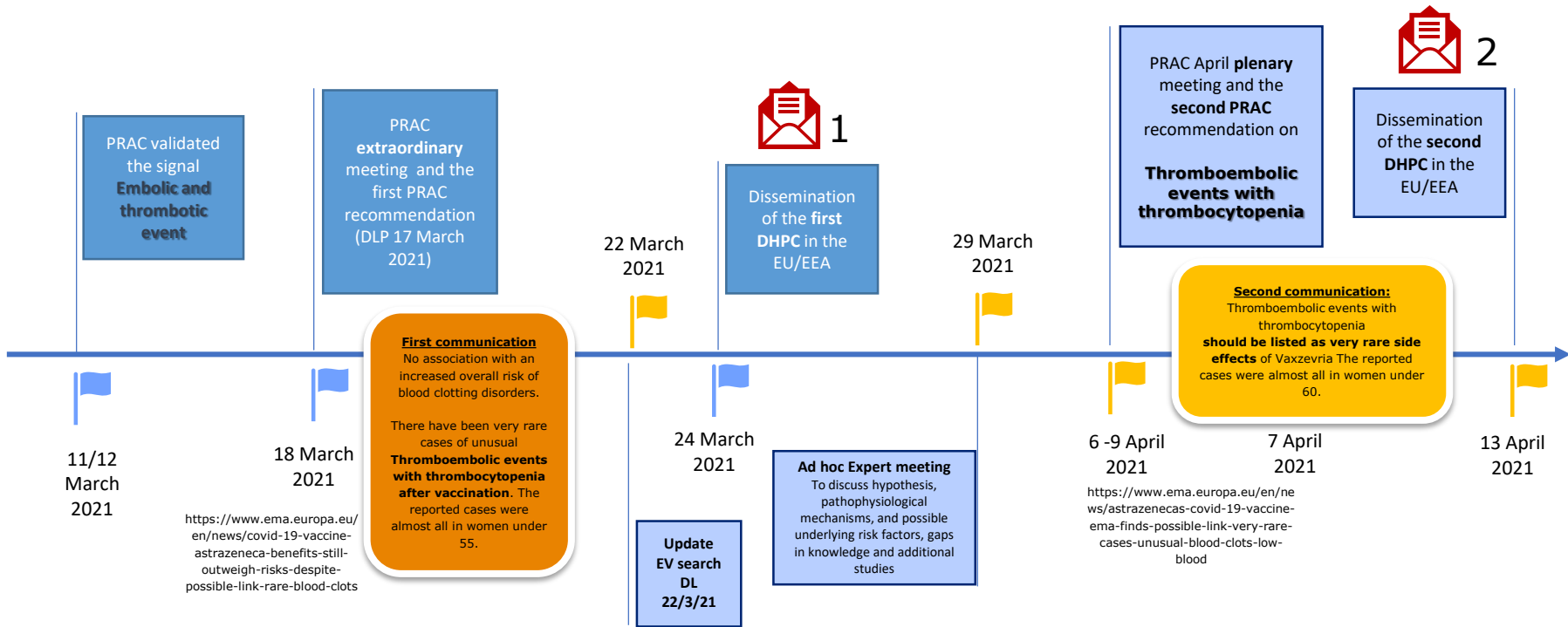
Significant increase Q1 2021:

- reporting of ADRs from the EEA non-EEA;
- number of ADR reports recoded in EV by EMA **increased almost 12 fold**
- reporting from patients **increased by 146%** compared to Q1 2020
- number of PhV queries received via Ask EMA **increased almost 2 fold**
- number of 'hits' on adrreports.eu **increased to 2.8 million** in Q1 2021 (2.5 million for the whole 2020)

- Cases picked up initially in unusual location (e.g. **CVST**, **Splanchnic Thrombosis**)
- Coagulation abnormalities in COVID19 are described as a consequence of cell and tissue damage
- Cases in EV appear similar to HIT-like syndrome: Platelet factor 4 is released to bind Heparin resulting in immunocomplex that aggregate platelets which induce thrombosis
- New clinical entity was identified **Thrombosis Thrombocytopenia Syndrome (TTS)**= platelets count decreased + thromboembolism
- Frequency: about **1/100.000** vaccinees
- Same risk was confirmed also for **Janssen**
- R/B + however **continuous monitoring** of the new cases + frequency



Exceptional EMA and Network Effort to rapidly detect, minimise, conclude and communicate on serious risks such as TTS





Council Regulation No 726/2004: EMA responsible for the scientific evaluation of applications for European Marketing Authorisation for medical products

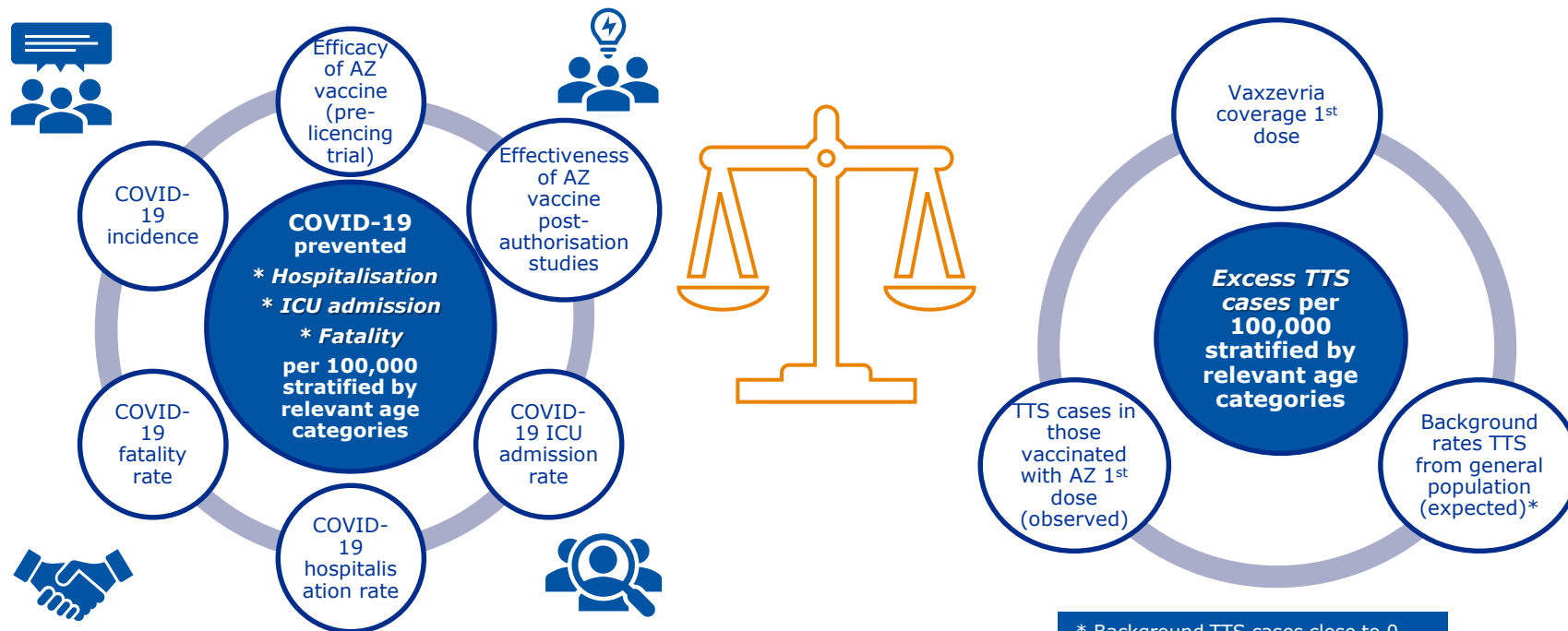
March 2021, signal assessment was initiated at EMA's Pharmacovigilance Risk Assessment Committee (PRAC) for embolic and thrombotic events with Vaxzevria

On 9 April 2021, EC triggered a procedure under Article 5(3) of Regulation (EC) No 726/2004 requested the Agency to perform a further analysis and stratification of data to contextualise the benefits and risks of the vaccine

7 April 2021, PRAC concluded a causal relationship between Vaxzevria and TTS (thrombosis in combination with thrombocytopenia). Most of these cases occurred in people under 55 years of age



Benefits of having AZ vaccine versus potential risks associated with AZ vaccine by relevant risk factors: contextualisation exercise (EU/EEA)





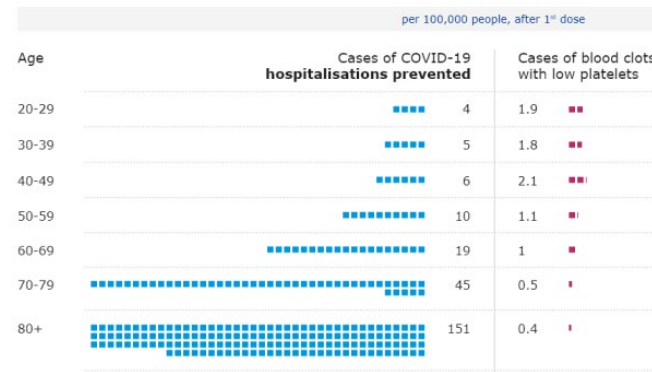
Visual benefit risk contextualisation

Medium infection rate*



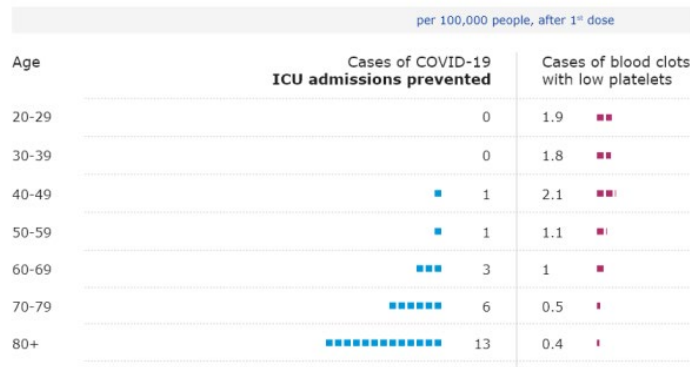
* "Medium" exposure: using virus circulation for March 2021 (incidence 401/100,000 population)

Low infection rate*



* "Low" exposure: using virus circulation for September 2020 (incidence: 55/100,000 population)

Low infection rate*



* "Low" exposure: using virus circulation for September 2020 (incidence: 55/100,000 population)

Benefits depending on age, infection rate and parameter of interest

Aim: To guide evidence based decision-making about COVID-19 vaccine indications, vaccination policies, and treatment options for pregnant women

Objectives:

- ✓ Assess **use of medicines** for COVID-19 treatment in pregnant women and compare with non-COVID-19/non-pregnant women of same age
- ✓ **Describe severity and clinical outcomes of COVID-19 disease** in pregnant women and compare to non-pregnant women of reproductive age with COVID-19
- ✓ To **assess and compare pregnancy and neonatal outcomes** in different treatment groups of pregnant women for COVID-19
- ✓ To **establish collaborations** with other global initiatives (ICMRA) and have sustainability
- [CONSIGN-INTERNATIONAL](#): Document outlining practical steps for international collaboration on meta-analyses
- More details: ENCePP news item dated 29/04/2021: [LINK](#)

Work Package 1 : Secondary use of real world data collected in health care DBs

Work Packages 2 ([COVI-PREG](#)) and 3 ([INOSS](#)): Primary data collection

[CDC study](#): Current status: Enrolment of 35 691 pregnant women in v-safe surveillance system and nearly 4000 in pregnancy registry – so far reassuring preliminary results on mRNA Covid-19 Vaccine Safety



Key Messages

- COVID-19 pandemic presents a major public health challenge – we are all committed to a common goal
- Unprecedented collaboration and unprecedented interest and scrutiny
- Regulators had risen to the challenge and demonstrated to have systems in place to rapidly detect any safety issues and minimise serious risks to patients
- Timely exchange of information, transparency and communication are critical
- **An unique opportunity and a privilege to contribute to public health**





Thank you for your attention

Further information

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