Monitoring the safety of COVID-19 vaccines using real-world data

PCWP-HCPWP joint meeting, Day 1

01 June 2021

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An agency of the European Union

From early times to expanding safety surveillance activities

2020 ACCESS project

Preparedness

Completed ☑

2021 Early study ★

- Incidence rates of adverse events
- 7 MSs + UK
- + monitoring in EU healthcare databases

2021-22 Future studies ★

- **EC funding**
- Active surveillance
- Signal strengthening
- Signal evaluation

Natural history of coagulopathy and use of anti-thrombotic agents (COVID-19 patients + persons vaccinated against SARS-CoV-2 ★

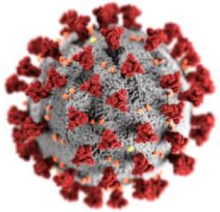
New tender: measuring the association (TE events & TTS)

★ Generation of background incidence rates

*TE: thromboembolic events
TTS: thrombosis with thrombocytopenia

2020 ACCESS

ACCESS

vACCine covid-19  monitoring readinESS

Completed ☑

- **Background rates of AESIs** from 7 databases in 5 countries: Spain, Italy, UK, Netherlands, Germany, Denmark (+ France available in June) (Link to report)
    - Interactive dashboard to visualise background rates: https://vac4eu.org/covid-19-tool/
- **Protocol templates for studies**: safety (Link) and effectiveness studies (Link); coverage of COVID-19 vaccines in healthcare databases (Link)
- **Feasibility** of using EU healthcare databases (Link to report)

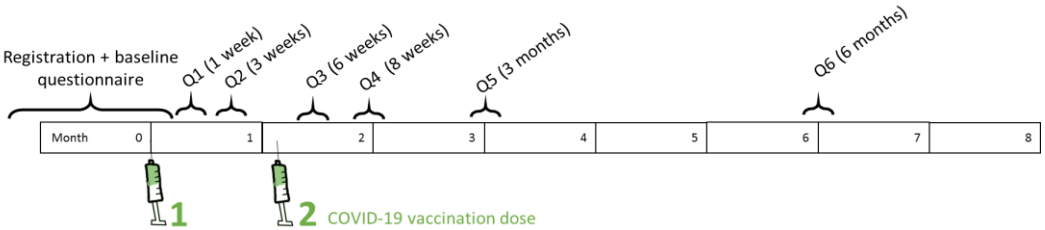
*AESIs: adverse events of special interest

Early safety monitoring study: Feb-Nov 2021

Two work packages:

1) Active surveillance, prospective cohort

- Vaccinated persons to self-report suspected adverse events using application (→ incidence data)
- Hypothesis-generating
- **7 MS** (Germany, Croatia, NL, Belgium, Luxembourg, Italy, France) + UK



2) Monitoring in electronic health records

- Databases in ES, IT, NL, UK
- AESIs and other adverse events, COVID diagnoses before/after vaccination, vaccinations
- Additional background rates for embolic and thrombotic events

Link to protocols on EU PAS Register
WP1 - WP2

Natural history of coagulopathy and use of anti-thrombotic agents in COVID-19 patients and in persons vaccinated against SARS-CoV-2

- Study initiated in 2020, data by Sept. 2021
- **Cohort of COVID-19 patients** : incidence rates of embolic and thrombotic events following COVID-19 infection
- **Vaccinated cohort** : incidence rates of embolic and thrombotic events within 7-, 14-, 21- and 28 days after vaccination
- Information on age, sex, vaccine, relevant risk factors (e.g. BMI, diabetes, hypertension, pregnancy, malignancy), medication use at time of vaccination
- Healthcare databases in 6 countries (DE, FR, ES, IT, NL, UK) – link to protocol: EUPAS40414

New study: Association between thrombosis with thrombocytopenia syndrome (TTS) or thromboembolic events, and COVID-19 vaccines

- Association not quantified so far. Objectives:

1) To quantify the association between occurrence of **TTS** and administration of a COVID-19

2) To quantify the association for **thromboembolic events**

3) To measure the **association** between potential **risk factors and TTS** in vaccinated patients

4) To describe **treatments** of patients with **TTS** (anticoagulants, other therapeutic products

Exploratory: To develop a proof-of-concept to support future genetic and pharmacogenomic analyses

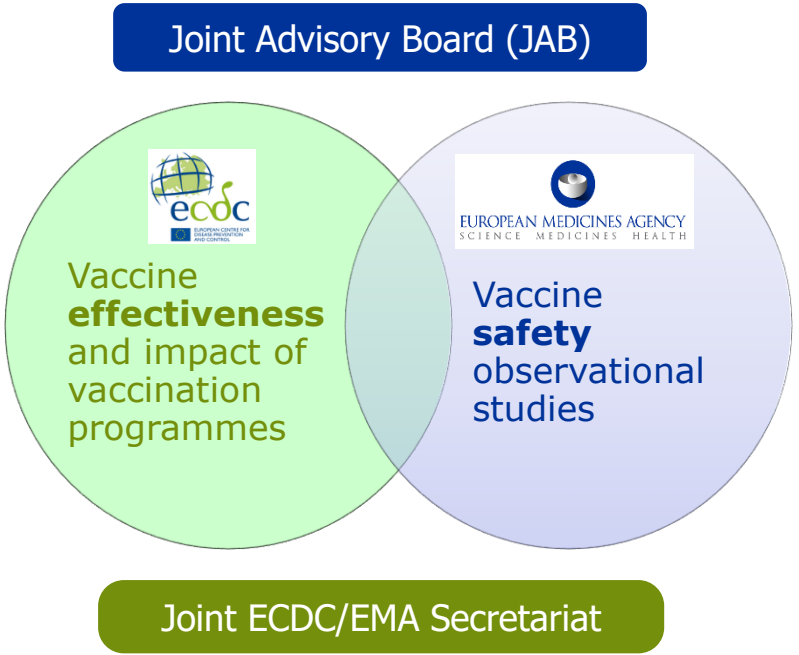
- In planning, data by early 2022

Joint ECDC/EMA COVID-19 vaccine monitoring platform

- EMA and ECDC extended mandate

→ European Health Union, joint coordination of independent vaccine monitoring activities

- Joint Advisory Board (EU Commission, national competent authorities, NITAGs*): prioritisation and advice on studies; appraisal of independent data
- Kick-off meeting 26 April 2021
- **Pilot to inform further establishment of sustainable EU platform, building on COVID-19 learnings**



*NITAGs: National Immunisation technical Advisory Groups

2021-22 EC-funded studies

EUROPEAN MEDICINES AGENCY

Two-year vaccine safety monitoring study

1) Active surveillance, prospective cohort

- Similar to early study + explore potential longer-term effects of the vaccines + suitable comparators
- At least 10 MSs not included in early study
- General population N≥60,000 (extension of early study)
- Special populations N=60,000 (from other EU projects, incl. children, pregnant women)

2) Readiness & rapid signal assessment

- Rapid pharmacoepidemiological analyses to characterise emerging safety concerns and support signal management
- Common data models, at least 10 electronic healthcare data sources (Netherlands, Denmark, Norway, Spain, Italy, France, Germany, UK)

Anticipated study start: July 2021

Can be adapted to emerging needs and monitoring of new events of interest

2021-22 EC-funded studies

EUROPEAN MEDICINES AGENCY

Preparedness for signal evaluation
→ Hypothesis-testing association studies

- Comprehensive pharmacoepidemiological studies to **measure the association** between COVID-19 vaccines and occurrence of specific safety concerns
- Provide **higher level of evidence**: comparisons at individual level, adjustment for confounders, stratification by variables of interest (e.g. risk factors)
- Relative risk (compared to non- vaccinated or other suitable comparator)
- Absolute risk (excess cases)

Covid-19 infectiON and medicineS In pregnancy (CONSIGN)

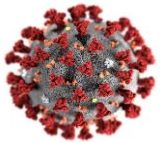
C  NSIGN

- Very little/no information to date as pregnant women mainly excluded from COVID-19 clinical trials

→ Guide evidence-based decision-making about COVID-19 vaccine indications, vaccination policies, and treatment options

- 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
  - ✓ To **establish collaborations** with other global initiatives (ICMRA) and have sustainability
- **Ultimately:** Worldwide infrastructure to study medicines in pregnancy beyond COVID-19

Info: LINK



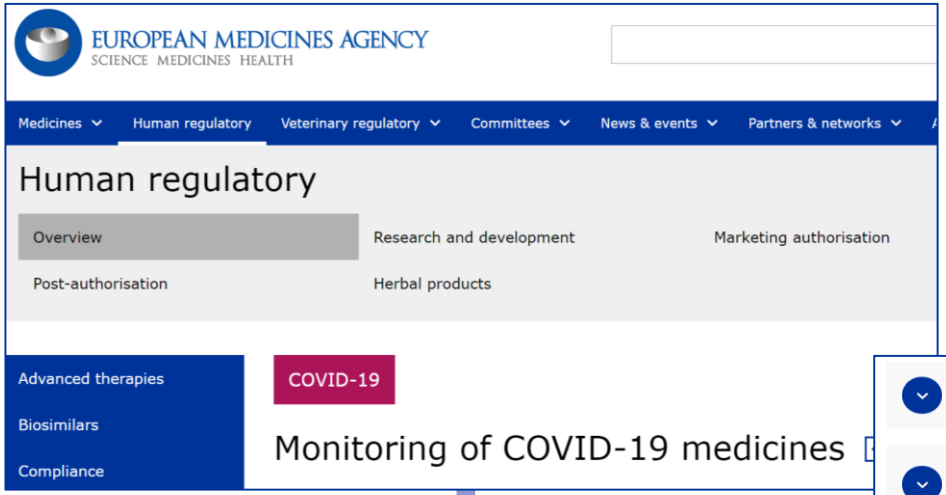
Lessons learned from preparedness activities

Challenges

- Background incidence rates of adverse events
- Quantifying associations between vaccines and adverse events
- Use of existing databases (data on vaccines, case validation, data source heterogeneity, time needed to obtain data, availability of lab data)
- Case definitions (TTS!)
- Impact of pandemic on healthcare systems

Opportunities

- Early preparation was absolutely needed (vaccination start in Dec. 2020)
- Prospective monitoring: apps, near-real time surveillance
- Value of large healthcare databases (sample size, hospital data, common data models, speedy analyses possible)
- Value of EMA framework contracts
- Consortia with demonstrated capacity/expertise
- International collaborations with other regulators
- Lessons learnt from H1N1 flu pandemic



Link to overview of observational COVID-19 research on the EMA website:

[Monitoring of COVID-19 medicines]

- Safety monitoring of COVID-19 vaccines in the EU (new)
- Natural history of coagulopathy and use of anti-thrombotic agents in COVID-19 patients and COVID-19 vaccine recipients
- Early safety monitoring of COVID-19 vaccines
- Impact of COVID-19 infection and medicines in pregnancy
- Building a framework for the conduct of multicentre cohort studies on the use of medicines in COVID-19 patients
- Preparing an infrastructure for the monitoring of the coverage, safety and effectiveness of COVID-19 vaccines

Thank you for your attention