The Cohorts Coordination Board (CCB) was developed based on the concepts that cohorts data during pandemic play a pivotal role

- In pandemic scenario most feasible design to explore risk factors, **genome associations, public health interventions, burden,** and **long term sequelae**
- Provide **early information to design randomised clinical trial (RCT)**
- **Essential role in data harmonisation and dictionary** among settings which increases data availability to assess research priorities for RCT
- Opportunity to select specific **subgroups** for RCT (hemato-oncological, recurrent infections, pregnant women..)
- Contribute to the **transferability of results from the RCT** in specific settings with difficulties in enrollment

SCOPE AND COMPOSITION of CCB

SCOPE

To create a running board comprising the most relevant international projects including cohorts of patients with SARS-CoV-2 infections

COMPOSITION

The CCB is organized in two levels:

- **a core group** (EC + EU funded project)
- **an extended group** (Policymakers, Scientific Experts and expert form Industry), who will be invited to participate as the need arises and according to the topic of discussion

Coordination: 5.1.2e & 5.1.2e

	CORE CCB
EC & Funded Projects	
ORCHESTRA	5.1.2e
END-VOC	
EUCARE	
CoVICIS	
European COVID-19 Data Platform	5.1.2e
RECODID	5.1.2e
SYNCHROS	5.1.2e
UNCOVER	
VERDI	5.1.2e
VACCELERATE	
EU Commission (obs)	
EU Commission (obs)	5.1.2e
EU Commission (obs)	5.1.2e
	EXTENDED CCB
Policymakers	
ECDC	5.1.2e
Regulators - Patients	
EMA	5.1.2e
EMA	
EFPIA	5.1.2e
Long COVID patients group	
Boards	
Trial Coordination Board	

COVID-19 Data Portal

Accelerating research through data sharing

Goal: to enable researchers to **upload, access and analyse** COVID-19 related reference data and specialist datasets as part of the wider European COVID-19 Data Platform.

Re CoD ID

Reconciliation of Cohort data in Infectious Diseases

Goal: to develop an quitable, acessible, and sustainable **model for the storage, curation, and analyses** of clinical- epidemiological and high- dimensional sample data collected by infectious disease cohorts in low- and- midle-income countries

VACCELERATE

European Corona Vaccine Trial Accelerator Platform - VACCELERATE Volunteer Registry

Goal: to speed up existing and upcoming development programmes as well as market authorisations for **new vaccines and vaccination strategies**

SYNCHROS

SYNergies for Cohorts in Health: integrating the ROle of all Stakeholders

Goal: to coordinate and support the **synchronisation of cohorts and population surveys** in Europe and worldwide

END-VOC

ENDing COVID-19 Variants Of concern through Cohort studies (END-VOC)

Goal: to elucidate **the global circulation** of the current and emerging SARS-CoV-2 VOCs and their characteristics and **how VOCs alter long- term post- infection sequelae** and where new VOCs emerge within hosts

unCoVer

Unravelling Data for Rapid Evidence-Based Response to COVID-19

Goal: to harvest **real- world data** derived from the response and provision of care to patients by the health systems across Europe, and internationally during the COVID-19 pandemic

European Cohorts of Patients and Schools to Advance Response to Epidemics

Goal: to confront the COVID-19 epidemics and, in particular, the **newly emerging SARS-COV-2 variants** under several aspects.

EU-Africa Concerted Action on SARS-CoV-2 Virus Variant and Immunological Surveillance

Goal: to couple powerful state-of-the-art virologic and immunologic platforms with **large genomic surveillance** studies and diverse cohorts in EU and SSA

SARS-CoV2 variants Evaluation in pRegnancy and paeDIatrics cohorts

Goal: to track and characterise variants of concern in **paediatric and pregnant populations** across the globe and to understand effects of variants of concern on clinical outcomes (short/longer term), vaccine effectiveness and transmission characteristics

Connecting European cohorts to to increase common and effective response to SARS-CoV2 Pandemic

Goal: to establish an **international large-scale cohort** for the conduct of retrospective and prospective studies in order to generate rigorous evidence to improve the prevention and treatment of COVID-19 and to be better prepared for future pandemics

CCB OBJECTIVES (I)

- Map **common tasks** across the cohorts
- Provide an update on the **status of ongoing cohort studies**, including defined outcomes and early results
- **Avoid overlapping and duplication of efforts** (not limited to cohort research but also in the creation of tools and infrastructures)
- **Combine forces** to achieve results driving improvements in clinical management of patients and prevention (e.g. **larger sample sizes**, stronger powered results, and wider dissemination)
- **Share approaches** to overcome common encountered obstacles (e.g. **shipment** of samples across national borders, lack of common **dictionaries**, electronic tools to link anonymous patient IDs to multiple samples and WPs, data standard and harmonisation)

CCB OBJECTIVES (II)

- Organize **training activities** for best practices within sub-working groups of interest
- **Share documents of relevance** for cohorts and with a view to greater harmonization (DPMs, Data Sharing Agreements, Material Sharing Agreements, Informed Consent)
- Make **recommendations to the European Commission** for future research in this area
- **Link efforts for future collaborative projects**
- Assess **sustainability** of running cohorts and possible **transferability of the tools and data** patients to other infectious diseases (antimicrobial resistance?)

THEMATIC AREAS OF INTEREST OF CCB

Research areas:

- **Long-Covid**
- **Impact of early therapies** (monoclonal and antivirals) on long COVID and breakthrough infections
- Treatment in immunocompromised patients
- Shared scoping question (e.g. new cases of severe acute hepatitis in children, MPX,..)
- Prevention in schools / VoC

Operational and technical areas:

- Process of central biobanks (**common virtual biobanking**)
- **Federated data platforms** for privacy preserving analytics
- Meta data sharing platforms (e.g. Maelstrom Research, DxConnect)
- Standardization, data dictionaries and interoperability of data (including lab data)
- **Establishment of "essential" data dictionary** for existing and future cohort studies

Cohort specific areas:

- Collaboration of cohorts to provide control groups for each other
- Sustainability of cohorts' infrastructure after projects' closure

Challenges of data sharing in European Covid-19 projects: a learning opportunity for advancing pandemic preparedness and response

Critical Area	Suggested Actions
Inconsistency in application of GDPR across Member States	Non-binding implementing rules / Code of conduct recognised by Member States
Stringent local legal and ethical requirements impeding rapid collection of data and analysis	Guidelines for application of GDPR in case of pandemic or major public health threat
Lack of common standards on data use, and data interoperability	Mandate standard terminologies and classifications in funding frameworks
Lack of agreement on the use of metadata standards	Catalogue the international use of metadata standards to empirically determine most common used standards, incentivize researchers for proper metadata documentation
Lack of standardised reporting on harmonisation procedures	Training and education on best practices in reporting harmonisation procedures / High-quality peer-review on publication reporting harmonisation outcomes
Multiple community-developed standards for interoperability	Development of meta-harmonization tools for interoperability between community developed standards
Poor digital literacy and data science skills of staff of data owners (hospitals etc.)	Institutional capacity building for staff and resources for IT infrastructure and strengthening of inter-institutional collaboration.
Standard funding frameworks do not always adapt well to projects formulated to address a pandemic	Devise alternative formats with a focus on collaborative and network aspects favouring complementarity as much as competitiveness
Barriers of sharing individual patient data for EHR and for some retrospective cohort data	Further development and investment in federated learning and analysis networks and technology
Broad informed consent for data sharing often not available	Make broad informed consent for future use of data mandatory as part of funding
Manipulation of data for pseudonymization/anonymization purposes may undermine its scientific value	Align any manipulation of data for pseudonymization purposes to the longitudinal characteristics of cohort studies concerned (i.e. temporal and location dimensions).
Retrospective harmonization is extremely labour-intensive	Dedicated funding for retrospective harmonization of valuable cohort data (selective) / Investment in future development of (AI-based) harmonization routines which are less labour-intensive.

ORCHESTRA

Connecting European Cohort to Increase Common and Effective Response to SARS-CoV-2 Pandemic

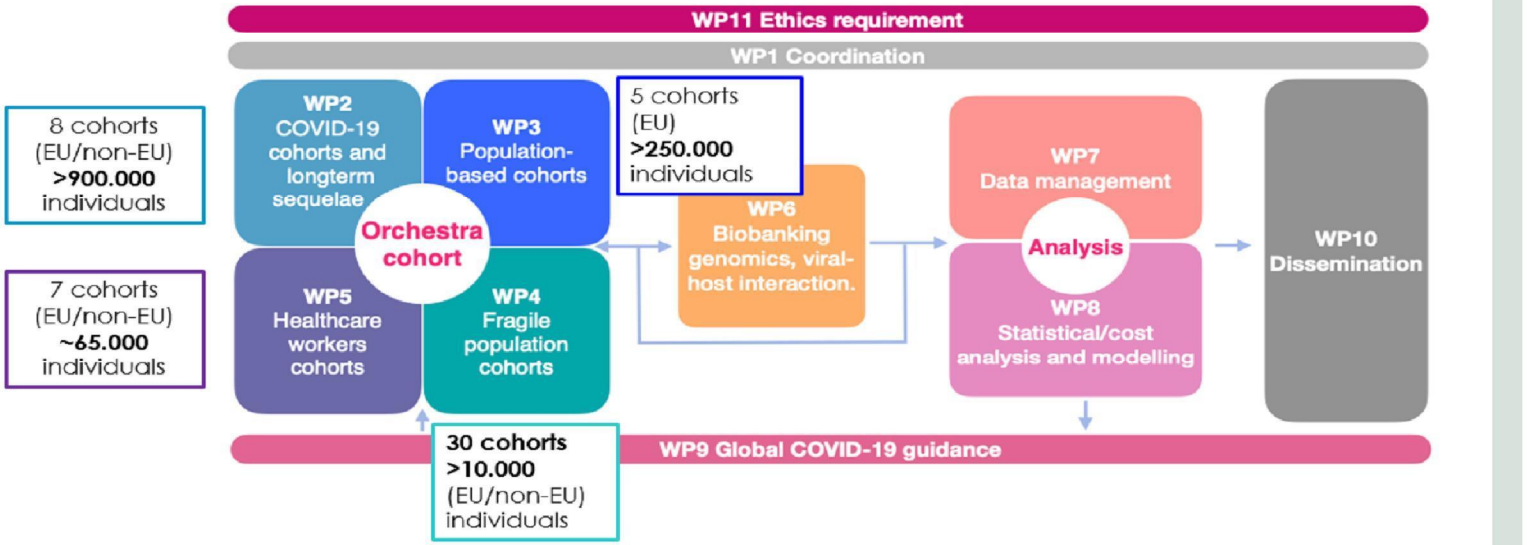
26 Partners from 10 European and 5 not European countries

7 linked and international Parties

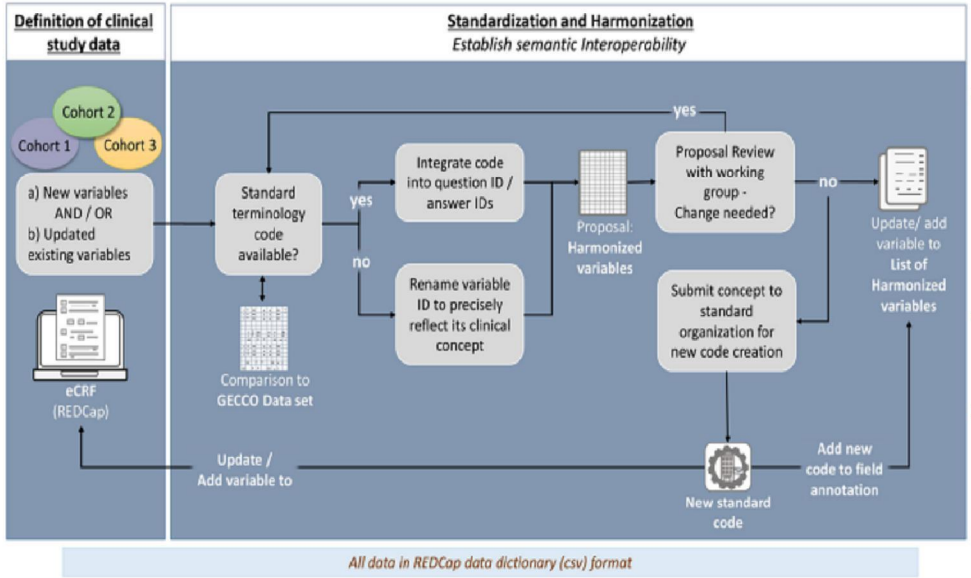
~ 1.300.000 individual patients' data

44 prospective cohorts

21 retrospective cohorts



Harmonization and standardization of data for a pan-European cohort on SARS- CoV-2 pandemic



- Consistent semantic representation of **over 2500 COVID-19-related variables were developed to define a common basis of standardized elements available for the design of new COVID-19 studies**
- 743 variables among retrospective cohorts were homogenised for comparison
- New concepts were sent to the terminology Standards Development Organizations

Rinaldi, Nature Digital Medicine 2022

Prospective cohort study for medium- and long-term follow-up in COVID-19 individuals

7 prospective cohorts
7443 patients included
1445 followed till 18 months of COVID-19 diagnosis
38559 samples collected

Type of analysis	Total samples	Samples at 31.10.2022				
		Acute phase	3M FU visit	6M FU visit	12M FU visit	18M FU visit
NP swabs (viral variants and resp microbiome)	**3869**	3380	328	142	13	6
Serology	**11 237**	4644	1762	2054	1617	1160
IFN-gamma	**5871**	2038	795	1298	1009	731
Cellular immunity (PBMCs)	**3063**	1039	351	727	528	418
Cytokines	**9208**	4062	974	1440	1580	1152
Epigenetics	**2039**	1454	302	159	96	28
Human genomics	**2097**	1466	328	176	97	30
Intestinal microbiome	**1175**	1003	169	3	0	0

Partners involved

Lead partners: UNIVR, INSERM, APHP

Other partners involved: all WP2 members, HMGU, ISGlobal

Clinical efficacy of different monoclonal antibody regimens among non-hospitalised patients with mild to moderate COVID-19 at high risk for disease progression: a prospective cohort study

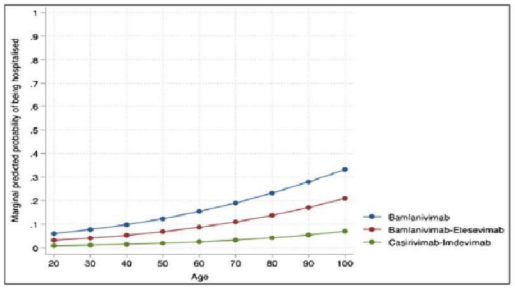


Fig. 1 Plots of marginal predicted probabilities of 28-day all-cause hospitalisation by age and mAb regimen

Clinical Impact of Monoclonal Antibodies in the Treatment of High-Risk Patients with SARS-CoV-2 Breakthrough Infections: The ORCHESTRA Prospective Cohort Study

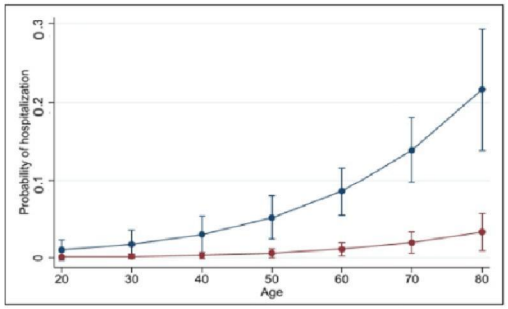


Figure 1. Marginal predicted probabilities of 28-day COVID-19-related hospitalization of outpatients treated with mAb by age and infection type: primary infection (blue curve) and breakthrough infection (red curve).

Savoldi and Tacconelli, EJCMID 2022; Bioemedicine 2022

Linking cohorts with RCTs: the example of the MANTICO RCT

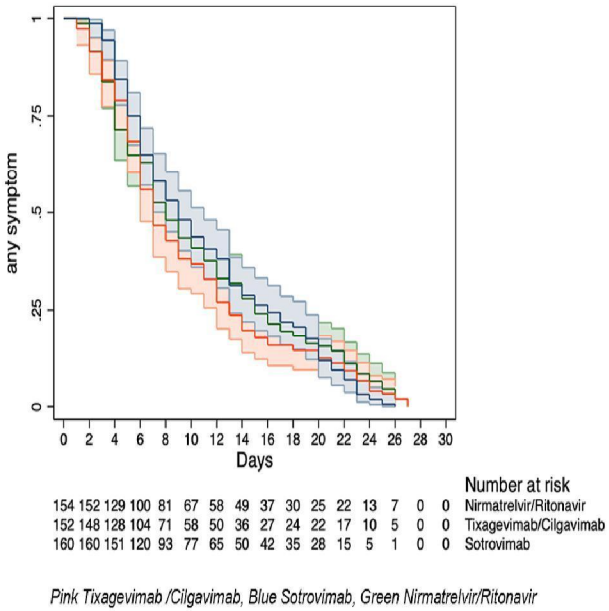
Exploratory data on the clinical efficacy of monoclonal antibodies against SARS-CoV-2 Omicron variant of concern

491 patients enrolled; > 95% Omicron BA.4 /5

Duration of symptoms - Median (CI): 8 days (7-9); (p = 0.57, log rank test)

- Tixagevimab /Cilgavimab: 7 days (6-9)
- Sotrovimab: 9 days (8-11)
- Nirmatrelvir/Ritonavir: 8 (7-10)

The MANTICO trial, born from the ORCHESTRA cohort, is the first RCT providing data on how the efficacy of monoclonal antibodies targeting SARS-CoV-2 varies according to the variant of concern

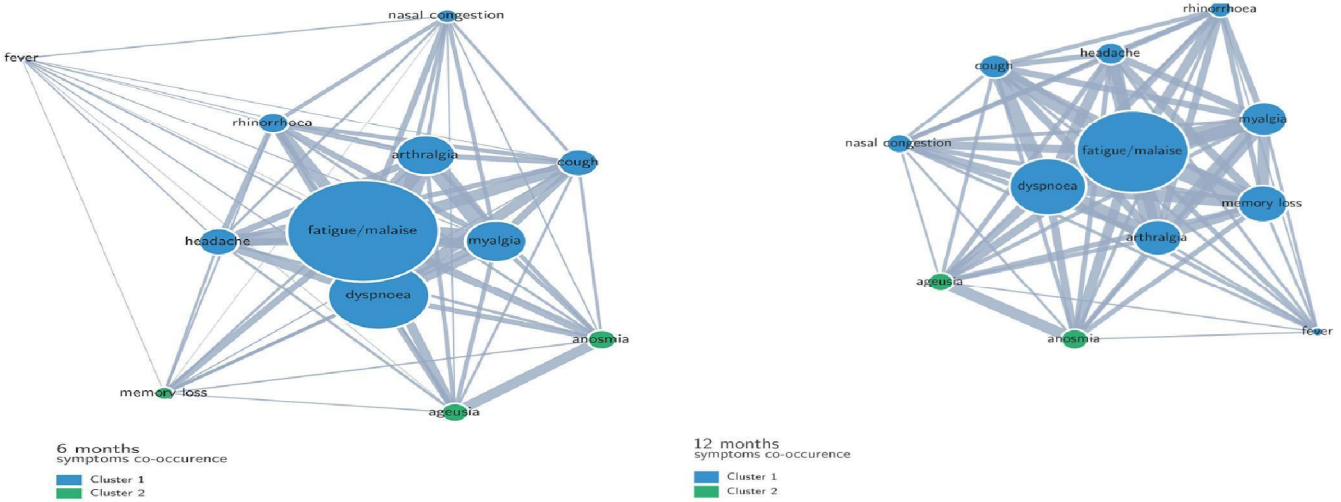


Pink Tixagevimab /Cilgavimab, Blue Sotrovimab, Green Nirmatrelvir/Ritonavir

Mazzaferri and Tacconelli eLife 2022

Clinical phenotypes and cluster of symptoms predicting long COVID

1796 patients followed up at 12-month: 1030 (57%) suffered from long COVID (WHO definition)



Cluster of symptoms by machine learning analyses at month-6 and month-12

Tacconelli, ORCHESTRA Deliverable WP2 2022

Clinical phenotypes and cluster of symptoms predicting long COVID

Using machine learning, symptoms were clustered into 4 clinical phenotypes defined as persistence of specific association of symptoms: respiratory cluster (RESc: cough and dyspnoea); chronic pain (CPc: arthralgia and myalgia); neurosensorial (NSc: alteration in taste and smell); chronic fatigue-like (CFSc: fatigue, headache and memory loss).

Logistic regression identified **different patterns of variables associated with each phenotype** (p<.001, all comparisons).

- Being females: CPc, NSc, and CPc.
- Chronic obstructive pulmonary disease: RESc.
- Neurological symptoms at diagnosis: RSc, NSc, and CFSc.
- Gastrointestinal symptoms at diagnosis: CFSc.

The anti-S Ab response was higher in patients in the RESc (13602 vs 12174 BAU; p=0.05) while patients in the NSc presented a lower anti-S Ab response (11307 vs 12436 BAU; p=0.03).

Early treatment of SARS-CoV-2 infection with monoclonal Ab reduced significantly the risk of all clinical phenotypes while vaccination had highest impact in reducing CFSc (p < 0.001).

Tacconelli, ORCHESTRA Deliverable WP2 2022

Next steps

- Define a system to support the sustainability of “perpetual cohorts” of patients after SARS-CoV-2 diagnosis
- The early definition of most relevant clinical, immunological, virological, and genomic phenotypes at higher risk of development of long COVID would inform design of RCT for new treatments and facilitate and improve enrollment (reducing the sample size needed to prove the hypothesis)
- The results from RCT would then be transferred to cohorts to facilitate follow up studies (adverse events, long term sequelae, impact on microbiome, burden of disease, cost-effectiveness of treatment etc..)
- The model could be a core component of preparedness plan and be applied to the infectious diseases emerging (MPX,…) or at highest burden in Europe (AMR, STD..)