

# Covid-19 effects on **ARTE**rial **Stiffness** and vascular **AgiNg** - (**CARTESIAN**) study

## 1° investigator meeting – 26/05/2020

Rosa Maria Bruno, Pierre Boutouyrie

INSERM U970; Université de Paris; Hôpital Européen Georges Pompidou – APHP, Paris, France

## CARTESIAN Study Investigator Meeting – 26/05/2020

# Agenda

- CARTESIAN update
- National Coordinator nomination
- Ethical Committee approval
- Artery Society Grant
- Data management
- Devices and standard operating procedures for vascular measurements

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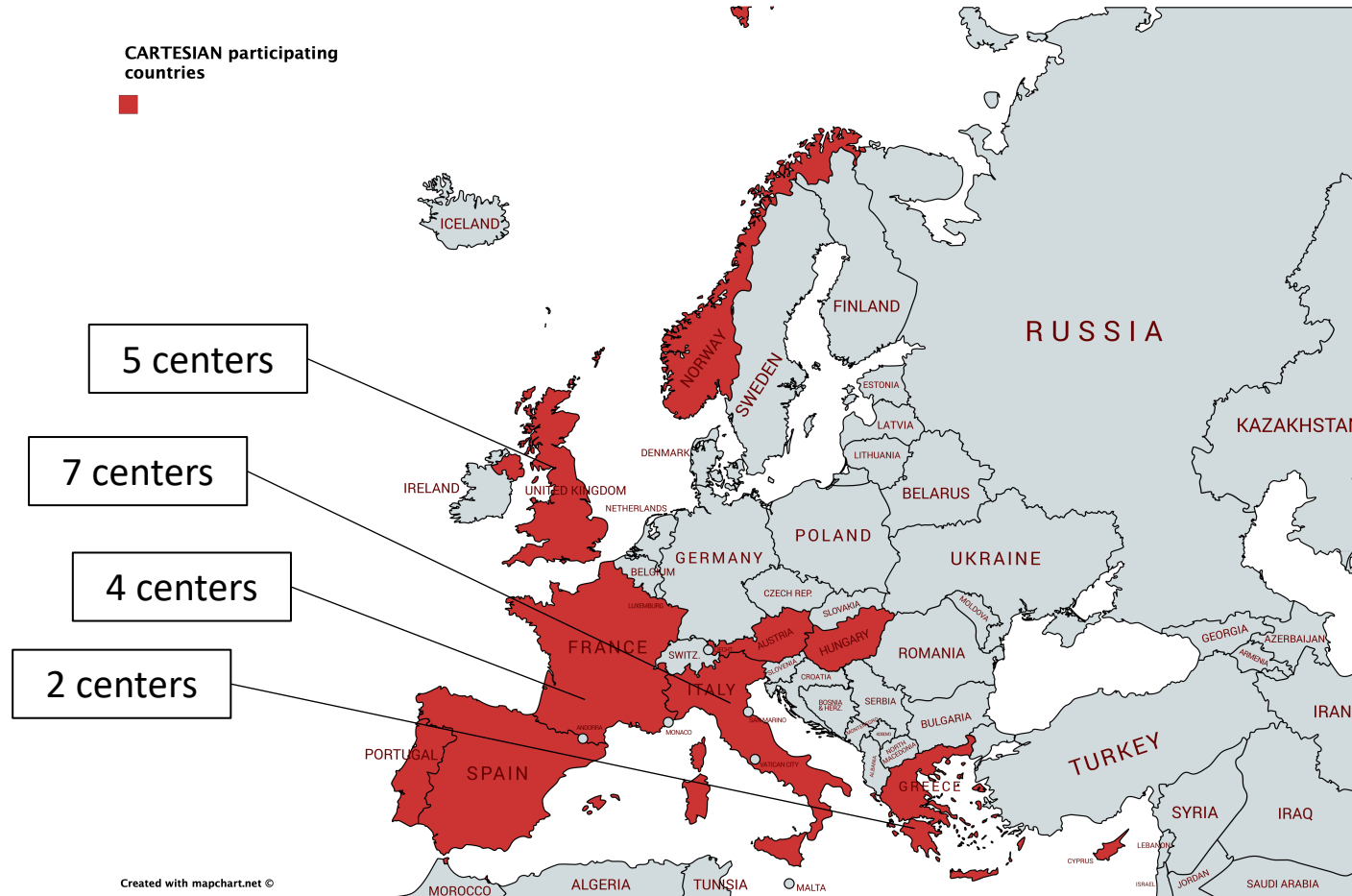
## CARTESIAN update: some numbers

- **32** participating centers
- **14** countries
- **2500** patients
- **4** supporting companies
- **60000** euro Grant from Artery Society
- **2** submitted grants (ANR France, BHF UK)
- **18216** Support from COST Action VascAgeNet
- **406** views on Facebook for the information session 19/05/2020



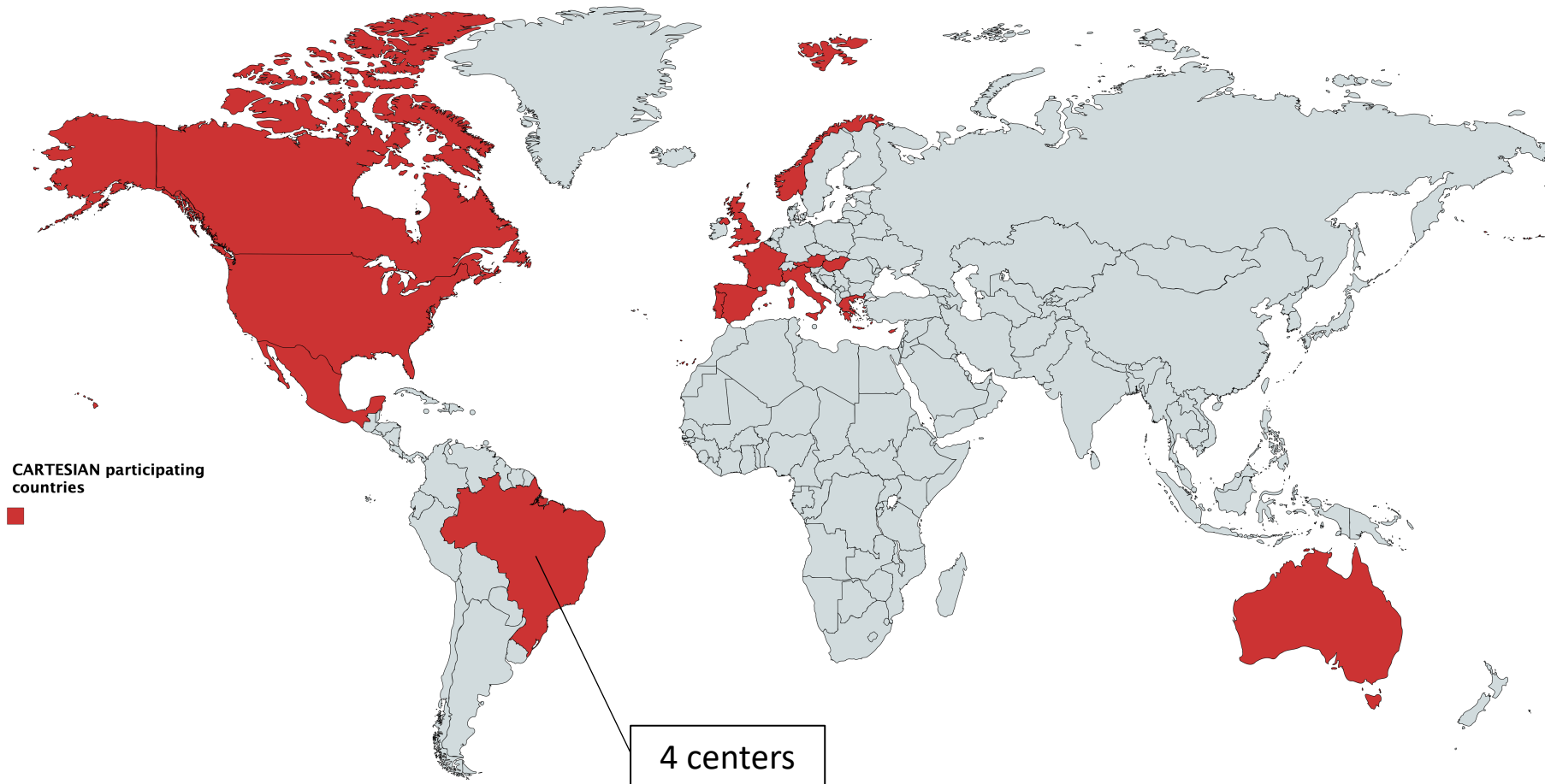
# CARTESIAN Study Investigator Meeting – 26/05/2020

## CARTESIAN update: participating centers



CARTESIAN Study Investigator Meeting – 26/05/2020

# CARTESIAN update: participating centers



# CARTESIAN Study Investigator Meeting – 26/05/2020

## CARTESIAN update

First Name	Last Name	Center (/!\ list on sheet "CENTER")
Pierre	BOUTOUYRIE	FRANCE - Paris -
Jeremy	BELLIEN	FRANCE - Rouen -
David	MONTAIGNE	FRANCE - Lille -
Athanase	BENETOS	FRANCE - Nancy -
Maria Lorenza	MUIESAN	ITALY - Brescia -
Lorenzo	GHIADONI	ITALY - Pisa -
Luca	ZANOLI	ITALY - Catania -
Davide	Grassi	ITALY - L'Aquila -
Andrea	Grillo	ITALY - Trieste -
Davide	Agnoletti	ITALY - Negrar -
Giacomo	Pucci	ITALY - Terni -
Alun	HUGHES	UK - London - UCL
Chakravarthi	RAJIKUMAR	UK - Brighton -
Riaz	AKTHAR	UK - Liverpool -
Kennedy	CRUICKSHANK	UK - London - KCL
Maria	Perissiou	UK - Portsmouth -
Jose	VILELA-MARTIN	Brazil - San Pualo -
Luiz	Bortolotto	Brazil - São Paulo -
Rogério	Okawa	Brazil - Parana -
Weimar	Kunz Sebba Barroso	Brazil - Goias -
Remi	Goupil	Canada - Quebec -
Carlos	Ramos-Becerra	Mexico - Jalisco -
Maria	Azancot	Spain - Barcelona -
Alvaro	Gurovich	United States - El Paso, Texas -
Lucimere	Bohn	Portugal - Porto -
Bela	BENCZUR	Hungary - Tolna Country -
Antonios	Argyris	Greece - Athens -
Andrie	panayiotou	Cyprus
Mai Tone	Lonnebakken	Norway

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## CARTESIAN Study Investigator Meeting – 26/05/2020

# National Coordinators

- France: Rosa Maria Bruno and Pierre Boutouyrie (Paris)
- UK: Alun Hughes (London) and Chakravarthi Rajikumar (Brighton)
- Italy: Maria Lorenza Muiesan (Brescia)
- Greece: Dimitrios Terentes-Printzios and Charalambos Vlachopoulos (Athens)
- Brazil: please show up and make a decision!
- Hungary, Greece, Spain, Portugal, Norway, Cyprus, US, Canada, Mexico, Australia: one center per country: you are the National Coordinator (reference for future participating centers)

# National Coordinator Tasks

- Is formally responsible for the study in his/her country (the CARTESIAN study is a consortium of national studies)
- Takes care of Ethics Committee submission and approval for his/her country
  - Prepares site-specific documents (patient questionnaires, informed content, study summary) in the country language and share them with the national centers
  - Transmits Ethics Committee approval document to the CARTESIAN PI
- Collects information about national centers (tests performed, devices and softwares availables and their version) and reports needs and problems to the CARTESIAN PI
- Launches and coordinates national initiatives: national grant proposals, link with national scientific societies, scientific / media communication ...

## CARTESIAN Study Investigator Meeting – 26/05/2020

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CARTESIAN Study Investigator Meeting – 26/05/2020

## Ethical Committee Approval

- Protocol and Informed Consent are ready (in English)
- CRF needs last refining (finished by the end of this week, hopefully)
- National coordinators will be given access to a Google Drive folder with the final documentation



## CARTESIAN Study Investigator Meeting – 26/05/2020

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CARTESIAN Study Investigator Meeting – 26/05/2020

## Artery Society Grant

- This year the annual Artery Society Meeting is taking place virtually
- The Executive Meeting decided to invest the saved money (around 60.000 Euro) in a collaborative project → this is how the CARTESIAN Study was born

### How it works?

- Each participating center will receive an email with a link to an online form
- First transfer (1000 Euro) will take place at project start (Ethical Committee Approval)
- Second transfer (variable amount depending on number of centers, availability of further funds) will take place upon recruitment of the 20<sup>th</sup> patient



Questions?

## CARTESIAN Study Investigator Meeting – 26/05/2020

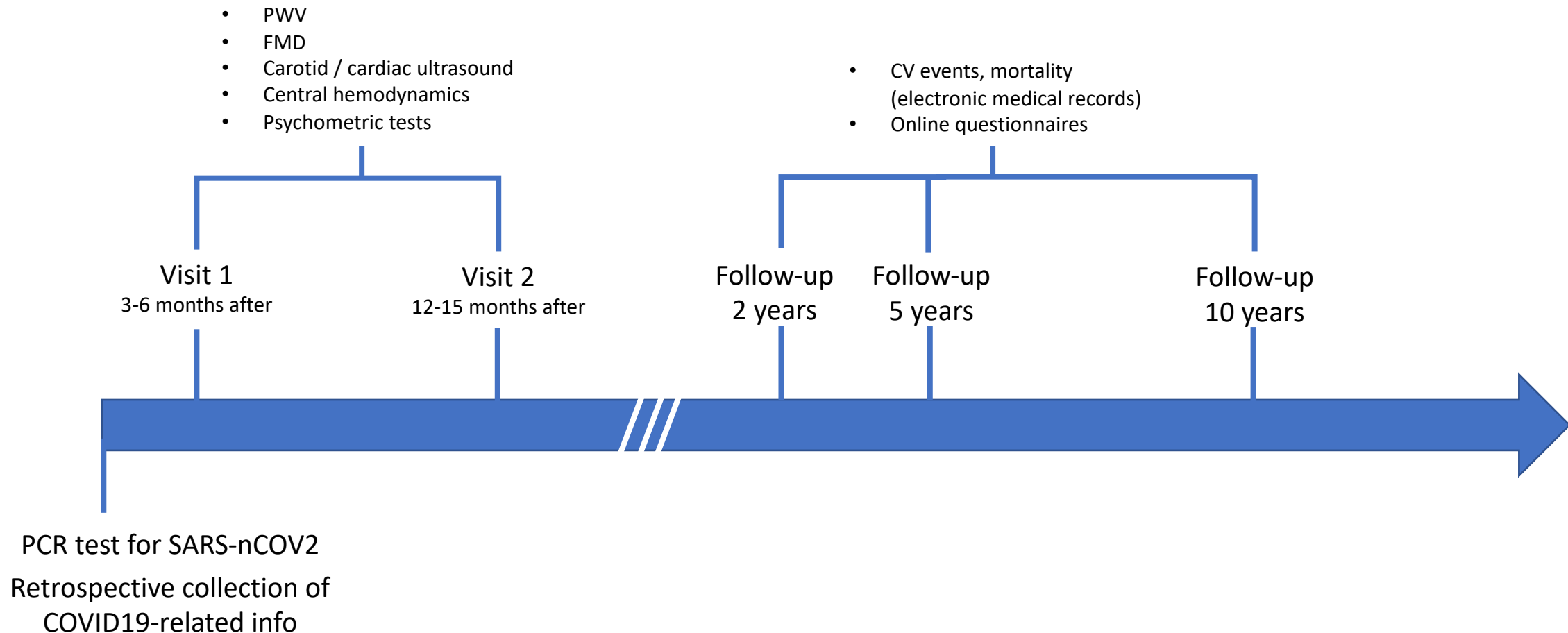
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# CARTESIAN Study Investigator Meeting – 26/05/2020

## Study design


- Prospective, multicenter study



# CARTESIAN Study Investigator Meeting – 26/05/2020

## Data management

- Electronic CRF on RedCap, hosted by INSERM, in the respect of GDPR for Europe
- Each participating center
  - will receive one or more username/password upon Ethical Committee approval
  - has access to his own data, the CARTESIAN PI have access all centers data
- Study protocol authorizes data transfer inside Europe



Logged in as **rosa-maria.bruno**  
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[Project Home](#) or [Project Setup](#)  
[REDCap Messenger](#)

Project status: **Development**

**Data Collection** [Edit instruments](#)

[Record Status Dashboard](#)  
- View data collection status of all records

[Add / Edit Records](#)  
- Create new records or edit/view existing ones

### ARTERY Covid19

#### **Add / Edit Records**



















You may view an existing record/response by selecting it from the drop-down lists below. To create a new record/response, type a new value in the text box below and hit Tab or Enter. To quickly find a record without using the drop-downs, the text box will auto-populate with existing record names as you begin to type in it, allowing you to select it.

**Total records: 1**

<b>Choose an existing Participant Identification Number (PIN):</b>	<input type="text" value="-- select record --"/>
<b>Enter a new or existing Participant Identification Number (PIN):</b>	<input type="text"/>

# CARTESIAN Study Investigator Meeting – 26/05/2020

## Data management

Instrument name	Fields	View PDF	Instrument actions
Participant Identification Number (PIN):	6		Choose action
Center-specific documents	18		Choose action
Inclusion Criteria	7		Choose action
Demographics	25		Choose action
Comorbidities	19		Choose action
Onset And Admission	17		Choose action
Admission Signs And Symptoms	44		Choose action
COVID19 Diagnosis	6		Choose action
Infectious Respiratory Disease Pathogen Testing	8		Choose action
Complications	28		Choose action
Treatment	26		Choose action
Outcome	8		Choose action
Core Additional Information	1		Choose action
Medical History	54		Choose action
Clinical Characteristics	24		Choose action
Vascular Tests (Mandatory)	21		Choose action
Vascular Tests (Optional)	44		Choose action
Pulsatile hemodynamics	1		Choose action
Questionnaires	133		Choose action




















3-digit center code +  
4-digit patient code

4 groups:

- 1) Patients with confirmed infection by SARS-Cov-2, requiring a hospitalization in intensive care unit
- 2) Patients with confirmed infection by SARS-Cov-2, requiring a hospitalization in a medicine unit
- 3) Patients with confirmed infection by SARS-Cov-2, not requiring hospitalization
- 4) individuals having performed a test for SARS-Cov-2 infection, but resulted to be negative

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Questionnaires	133		Choose action ▾

**Q: I see only hospitalized patients, can I recruit only group 1 and 2?**

**A:** Make all possible efforts to have a balanced recruitment. Please look for collaboration to your virology lab to have access to positive non-hospitalized / negative patients. Consider also relatives/contacts of positive cases and healthcare providers.




















**Q: May I include patients with very high suspicion of COVID-19 (typical CT scan + positive contact) but with a negative test?**

**A:** They are screening failures, they will not be included in the principal analysis; possibly in the future ones (serological confirmation?)  
- Mark in the Pathogen testing section that they have negative test  
**THUS ..** When recruiting, give priority to positive patients



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Questionnaires	133		<a href="#">Choose action ▾</a>

This section:



















- is about COVID-related characteristics
- is a simplified version of the WHO-ISARIC CRF
- should be filled at V1

If you are already participating to a study using the WHO-ISARIC CRF and you have the right to export those data, you do not need to fill in this part.

Simply annotate the patient ID in that cohort in the PIN section, together with the CARTESIAN ID.

# CARTESIAN Study Investigator Meeting – 26/05/2020

## Data management



















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This section:

- is about cardiovascular comorbidities and treatments
- should be filled at V1 and V2

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











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Vascular Tests (Optional)	44		Choose action ▾
Pulsatile hemodynamics	1		Choose action ▾
Questionnaires	133		Choose action ▾

This section:

- includes mandatory vascular tests
  - Carotid-femoral PWV
  - Central BP (tonometry)
- should be filled at V1 and V2

# CARTESIAN Study Investigator Meeting – 26/05/2020

## Data management




















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Vascular Tests (Mandatory)	21		Choose action ▾
Vascular Tests (Optional)	11		Choose action ▾
Pulsatile hemodynamics	1		Choose action ▾
Questionnaires	133		Choose action ▾

This section:

- includes optional vascular tests:
  - Carotid IMT and distensibility
  - Flow-mediated dilation
  - 24-h brachial and central BP
  - Cardiac ultrasound
  - Radial and digital IMT and distensibility
- should be filled at V1 and V2

# CARTESIAN Study Investigator Meeting – 26/05/2020

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CORE LAB for pulsatile hemodynamics analysis:  
AIT (Austria), Responsible: Christopher Mayer

We are defining a protocol for raw data export and transmission to the Core Lab.




















Upload of single patient data or entire center dataset can be done through the RedCap platform

→ Details will follow

This section is relative to aortic waveform raw data collection.

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- Questionnaires about socioeconomic status and psychological aspects are for self-administration
- They will be administered as paper questionnaires (ask your patients to bring a pen and glasses!).
- We are evaluating the option of generating an online questionnaire (to be sent by email or filled in on a tablet at the vascular lab)
- Questionnaires need to be translated in your country language.
- For standardized scales, validated versions must be used.
- Some of the chosen scales have copyright: a decision will be taken soon about using them (and pay rights to the authors) or replacing them.



Questions?

## CARTESIAN Study Investigator Meeting – 26/05/2020

# Agenda

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- Data management
- **Devices and standard operating procedures for vascular measurements**



## CARTESIAN Study Investigator Meeting – 26/05/2020

### Devices and SOP: carotid PWV

- Devices requested: Sphygmocor, Complior and PulsePen
- Atcor will support centers without validated devices with Sphygomor equipment for the duration of the study (3 centers already put in contact)
- 3 measures in the supine position (at least 10')
- Direct distance\*0.8

## CARTESIAN Study Investigator Meeting – 26/05/2020

### Devices and SOP: central BP and hemodynamics

- Devices requested: Sphygmocor device
- Validation with brachial BP is crucial: each center must have a validated brachial BP oscillometric device
- Atcor will support centers by updating software version and providing instructions for raw data export
- 3 brachial BP measurements (supine position for at least 10')
- 3 radial tonometry measurements

# CARTESIAN Study Investigator Meeting – 26/05/2020

## Devices and SOP: carotid IMT and distensibility

- Optional measurement
- Devices requested:
  - Any ultrasound machine with a linear probe 7.5-12 MHz able to save and export 10'-B-mode clips at adequate frame rate (20/s or more)
  - Image analysis software (Cardiovascular Suite-Carotid studio)
  - Tonometer for carotid pressure, validate oscillometric BP device
- Quipu srl will support interested centers by providing free demo licences for Cardiovascular Suite – Carotid Studio for the study duration and providing online training and assistance during the study
- Brachial BP and carotid tonometry immediately before the measurement
- 2 10'-clips right and left common carotid artery (1 cm from the bulb) (supine position for at least 10'), stored
- Offline clip analysis (Cardiovascular Suite-Carotid studio)

# CARTESIAN Study Investigator Meeting – 26/05/2020

## Devices and SOP: flow-mediated dilation

- Optional measurement (only for centers who have already experience with this technique!!!)
- Devices requested:
  - Ultrasound machine with a linear probe 7.5-12 MHz and duplex option
  - Image analysis software (Cardiovascular Suite-FMD studio)
  - Probe holder and frame grabber
  - Manual sphygmomanometer with pediatric BP cuff
- Quipu srl will support interested centers by providing free demo licences for Cardiovascular Suite – FMD Studio for the study duration and providing online training and assistance during the study
- Brachial artery diameter and flow-velocity simultaneous recordings (shear rate)
- 1'-baseline → 5'-ischemia → 4'-peak and recovery – continuous recordings

## CARTESIAN Study Investigator Meeting – 26/05/2020

### Devices and SOP: 24h-Blood Pressure Measurement (including PWA)

- Optional (logistics might be difficult)
- Devices requested: Mobil-O-Graph PWA (I.E.M., Stolberg, Germany)
- I.E.M. will support interested centers by providing free devices for the study duration
- 24 hour ABPM will be taken in all patients during regular daily life
- 15-20 minutes intervals of measurement between 6:00 am and 10:00 pm, 30 minutes intervals of measurement between 10:00 pm and 6:00 am
- At least 70% valid measurements to be acceptable
- Raw data export – central repository

## CARTESIAN Study Investigator Meeting – 26/05/2020

### Devices and SOP: Cardiac ultrasound

- Optional
- Devices requested: any ultrasound machine with cardiac probe
- Standard measurements of LV geometry, diastolic and systolic function
- Recording of aortic flow velocities and diameter clips for future analysis

## CARTESIAN Study Investigator Meeting – 26/05/2020

### Devices and SOP: Thoracic aorta calcifications

- Optional
- Devices requested: none
- Retrieve and score (semiquantitatively) thoracic CT scans performed for clinical reasons

### Devices and SOP: Radial and digital IMT and distensibility

- Optional
- Devices requested: VevoMD (Visualsonics) → Paris and Rouen (FR)
- Visualsonics will provide an additional 22MHz probe



Questions?



# Thank you for the attention!



