EU SolidAct

A pan-European adaptive platform study for COVID-19 and future pandemics

Kick-off meeting

Oslo University Hospital

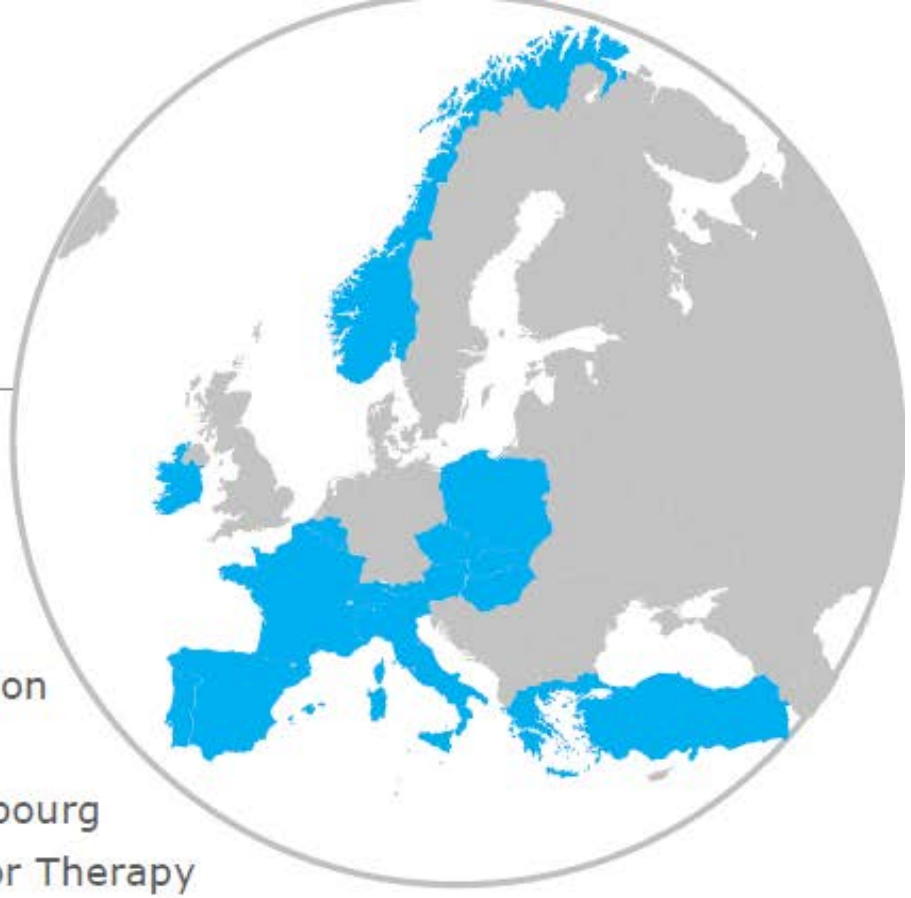
Part of EU-RESPONSE

EU SOLIDACT

Overview

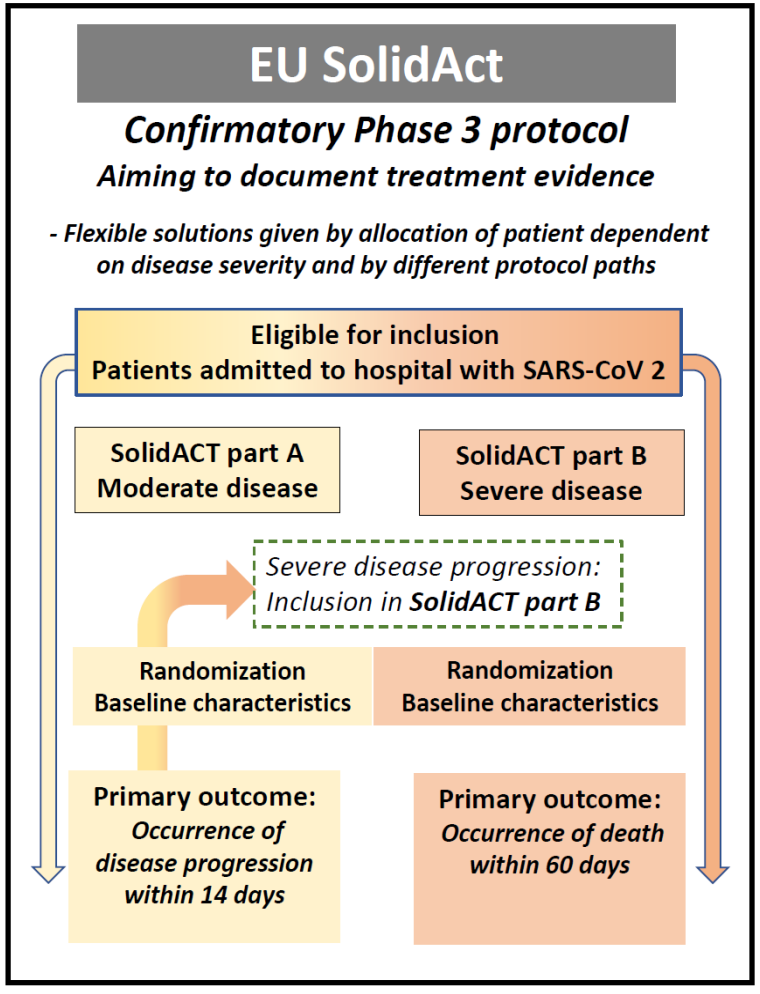
1. Introduction to the master protocol and sub protocol
2. Inclusion and exclusion criteria
3. Medications/drug handling
4. Monitoring/site initation
5. Brief introduction to eCRF
6. Safety (separate presentation)

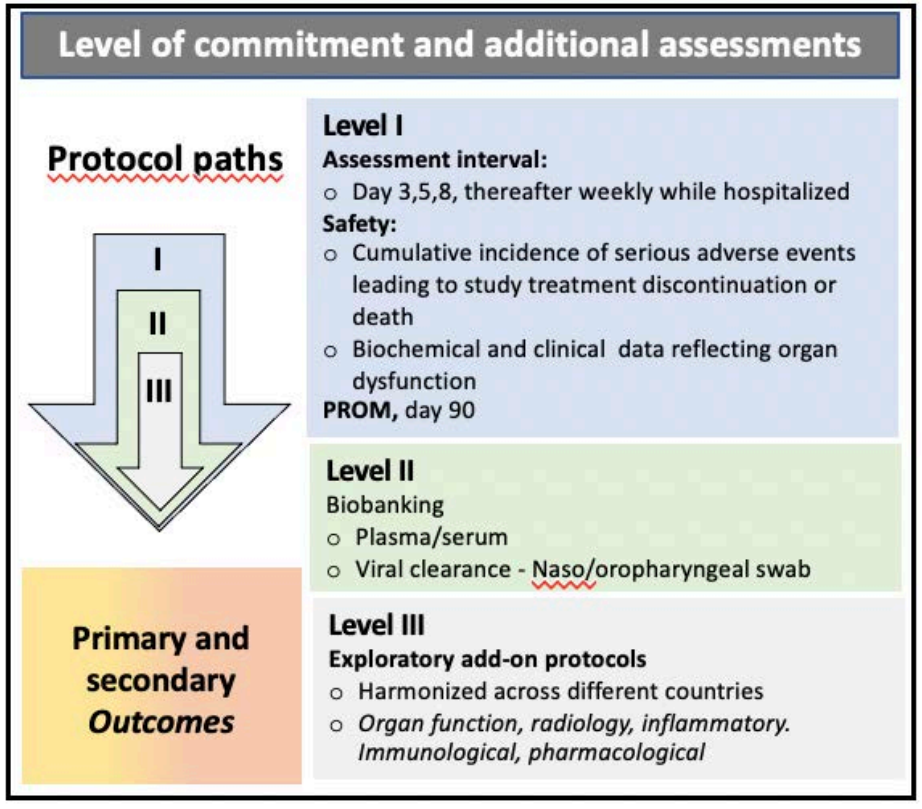
EU RESPONSE



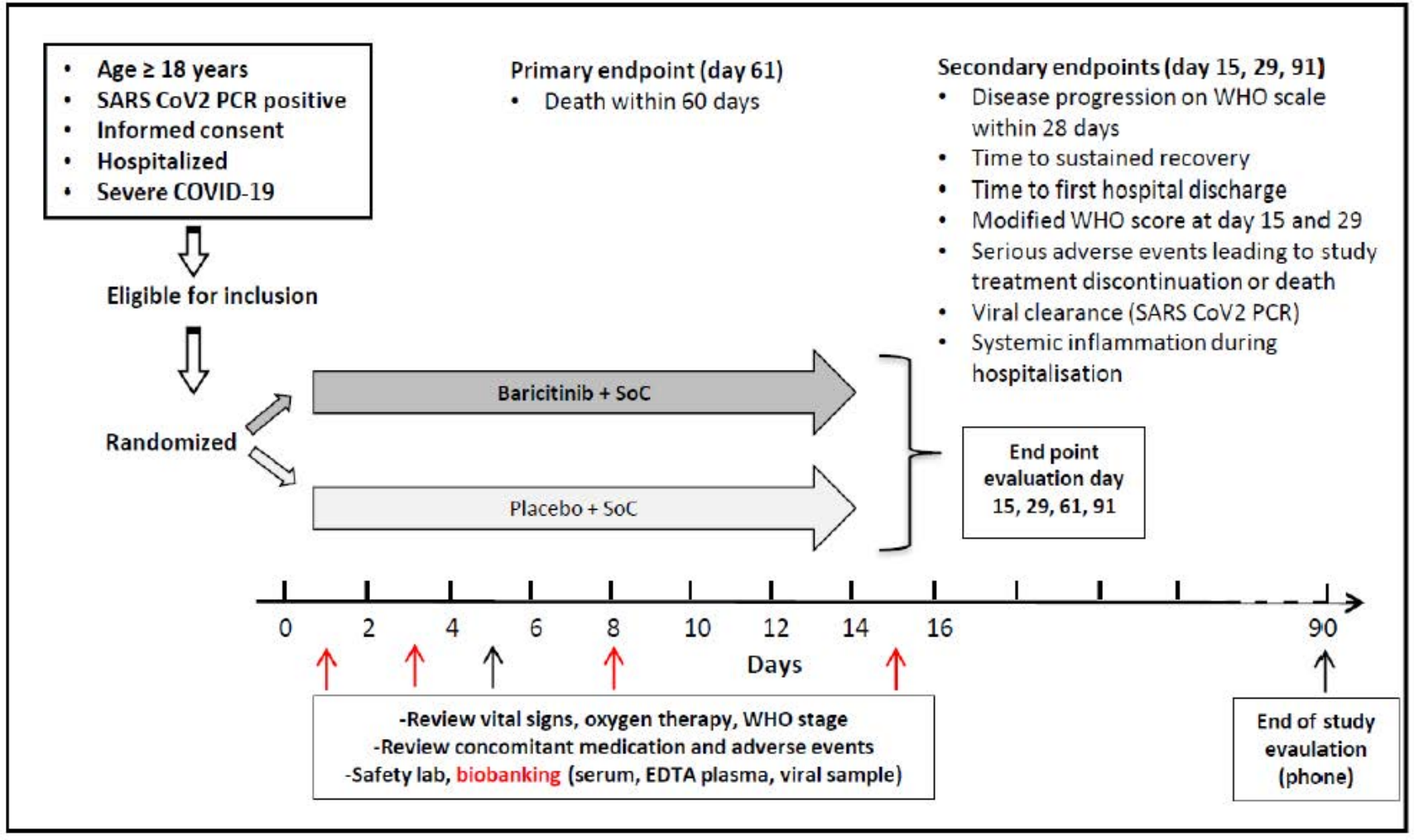
1. **INSERM**
   INSERM - PRC
   INSERM - U1137 IAME
   INSERM - U1111
   INSERM – U1136
2. ECRIN
3. Norwegien institute of Public Health
4. Oslo University Hospital
5. Università degli Studi di Verona
6. Centro Hospitalar Universitário Sao Joao
7. Inserm Transfert
8. Pavol Jozef Safarik University in Kosice
9. Université Libre de Bruxelles
10. University of Szeged
11. University College Cork
12. Swiss Clinical Trial Organisation
13. Hacettepe Üniversitesi
14. Centre Hospitalier de Luxembourg
15. Austrian Group Medical Tumor Therapy
16. APHP
17. Hospices Civils de Lyon
18. Servicio Madrileños De Salud
19. National and Kapodistrian University of Athens
20. Medical University of Lodz
21. Charles Univerzity

EU SolidAct Master Protocol





First Phase 3 Trial in EU - SolidAct Part B



Oslo University Hospital

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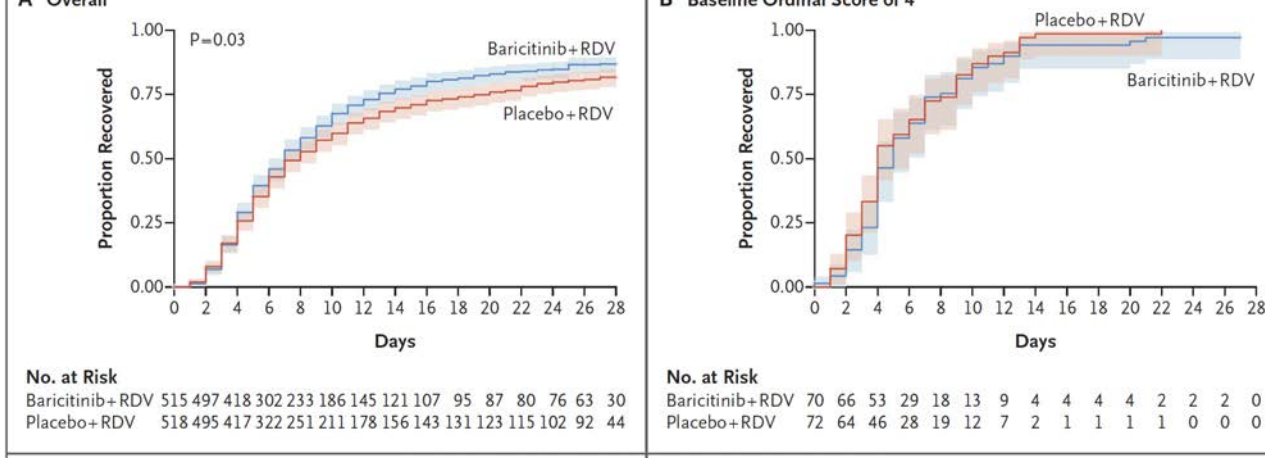
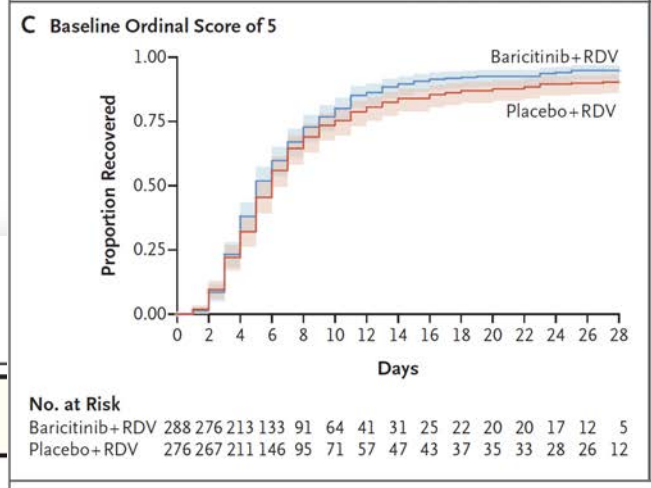
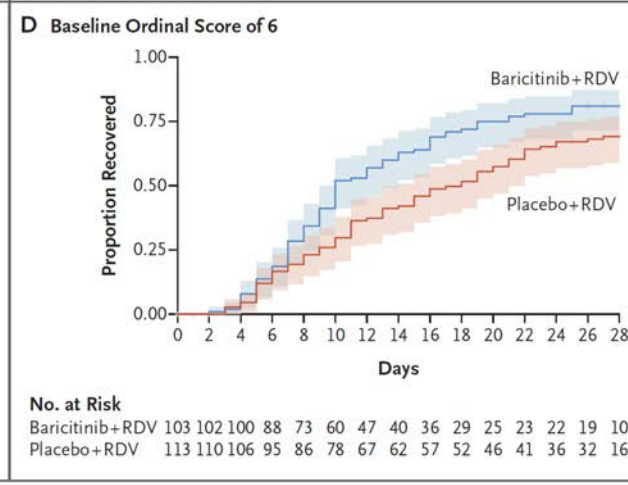
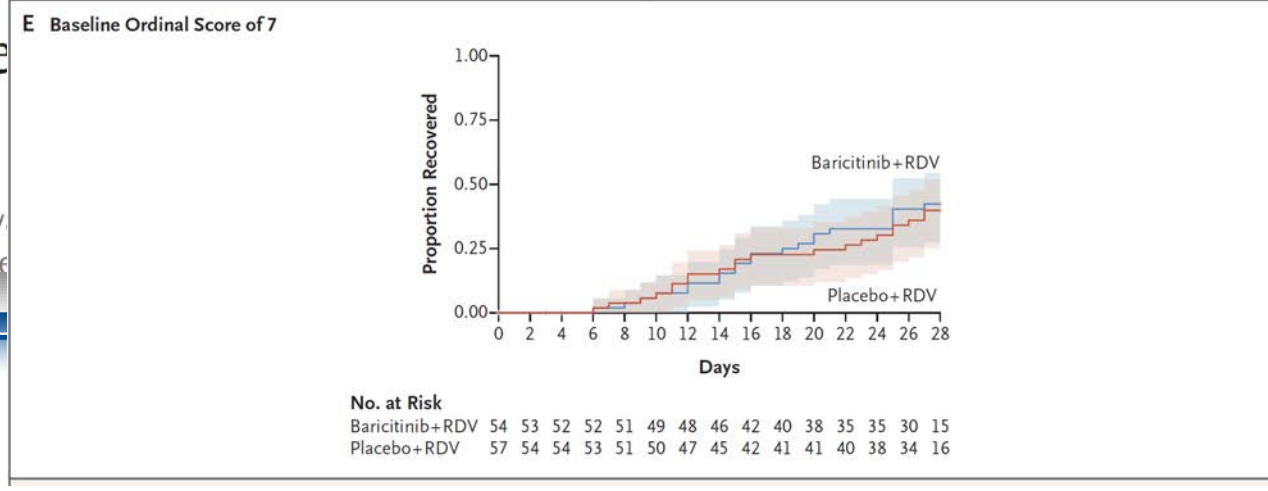
ACTT-2

- Remdesivir + baricitinib VS remdesivir + placebo









The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Baricitinib plus Remdesivir for Hospitalize Adults with Covid-19

A.C. Kalil, T.F. Patterson, A.K. Mehta, K.M. Tomashek, C.R. Wolfe, V. Ghazary V.C. Marconi, G.M. Ruiz-Palacios, L. Hsieh, S. Kline, V. Tapson, N.M. Iovine

Oslo University Hospital

Efficacy and safety of baricitinib for the treatment of hospitalised adults with COVID-19 (COV-BARRIER): a randomised, double-blind, parallel-group, placebo-controlled phase 3 trial

*Vincent C Marconi, Athimalaipet V Ramanan, Stephanie de Bono, Cynthia E Kartman, Venkatesh Krishnan, Ran Liao, Maria Lucia B Piruzeli, Jason D Goldman, Jorge Alatorre-Alexander, Rita de Cassia Pellegrini, Vicente Estrada, Mousumi Som, Anabela Cardoso, Sujatro Chakladar, Brenda Crowe, Paulo Reis, Xin Zhang, David H Adams, E Wesley Ely, on behalf of the COV-BARRIER Study Group**

Summary

Background Baricitinib is an oral selective Janus kinase 1/2 inhibitor with known anti-inflammatory properties. This study evaluates the efficacy and safety of baricitinib in combination with standard of care for the treatment of hospitalised adults with COVID-19.

Methods In this phase 3, double-blind, randomised, placebo-controlled trial, participants were enrolled from 101 centres across 12 countries in Asia, Europe, North America, and South America. Hospitalised adults with COVID-19 receiving standard of care were randomly assigned (1:1) to receive once-daily baricitinib (4 mg) or matched placebo for up to 14 days. Standard of care included systemic corticosteroids, such as dexamethasone, and antivirals, including remdesivir. The composite primary endpoint was the proportion who progressed to high-flow oxygen, non-invasive ventilation, invasive mechanical ventilation, or death by day 28, assessed in the intention-to-treat population. All-cause mortality by day 28 was a key secondary endpoint, and all-cause mortality by day 60 was an exploratory endpoint; both were assessed in the intention-to-treat population. Safety analyses were done in the safety population defined as all randomly allocated participants who received at least one dose of study drug and who were not lost to follow-up before the first post-baseline visit. This study is registered with ClinicalTrials.gov, NCT04421027.

Findings Between June 11, 2020, and Jan 15, 2021, 1525 participants were randomly assigned to the baricitinib group (n=764) or the placebo group (n=761). 1204 (79·3%) of 1518 participants with available data were receiving systemic corticosteroids at baseline, of whom 1099 (91·3%) were on dexamethasone; 287 (18·9%) participants were receiving remdesivir. Overall, 27·8% of participants receiving baricitinib and 30·5% receiving placebo progressed to meet the primary endpoint (odds ratio 0·85 [95% CI 0·67 to 1·08], p=0·18), with an absolute risk difference of −2·7 percentage points (95% CI −7·3 to 1·9). The 28-day all-cause mortality was 8% (n=62) for baricitinib and 13% (n=100) for placebo (hazard ratio [HR] 0·57 [95% CI 0·41–0·78]; nominal p=0·0018), a 38·2% relative reduction in mortality; one additional death was prevented per 20 baricitinib-treated participants. The 60-day all-cause mortality was 10% (n=79) for baricitinib and 15% (n=116) for placebo (HR 0·62 [95% CI 0·47–0·83]; p=0·0050). The frequencies of serious adverse events (110 [15%] of 750 in the baricitinib group *vs* 135 [18%] of 752 in the placebo group), serious infections (64 [9%] *vs* 74 [10%]), and venous thromboembolic events (20 [3%] *vs* 19 [3%]) were similar between the two groups.

Lancet Respir Med 2021

Published Online September 1, 2021 https://doi.org/10.1016/S2213-2600(21)00331-3

See Online/Comment https://doi.org/10.1016/S2213-2600(21)00358-1

For the French translation of the abstract see Online for appendix 1

For the Japanese translation of the abstract see Online for appendix 2

For the Portuguese translation of the abstract see Online for appendix 3

For the Russian translation of the abstract see Online for appendix 4

For the Spanish translation of the abstract see Online for appendix 5

*Members listed in appendix 6 (pp 2–5)

Emory University School of Medicine, Rollins School of Public Health and the Emory Vaccine Center, Atlanta, GA, USA (Prof V C Marconi MD); **Atlanta Veterans Affairs Medical Center, Decatur, GA,**

Patient Inclusion

Inclusion and Exclusion Criteria
Informed Consent

Inclusion Criteria

- ≥18 years old
- Confirmed SARS-CoV-2 infection with positive PCR last 9 days
- Admitted to hospital
- Informed consent, personally or via relatives
- Severe illness, defined as at least one of the following:
  - SpO_2 <90 % on room air
  - SpO_2 90 – 94 % and deteriorating condition or respiratory distress
  - Requires NIV, high-flow oxygen or mask with reservoir
  - Requires mechanical ventilation or ECMO

Exclusion Criteria

- **Expected transfer to a hospital** that is not taking part in the study within the next 72 hours.
- Use of **cytotoxic or biological treatments**
  - B-cell-corrected therapy shall not have been given within 24 weeks or 5 half/lives (whichever is longer)
  - TNF-inhibitors shall not have been given within 2 weeks or 5 half-lives (whichever is longer)
  - JAK-inhibitors shall not have been given within 1 week or 5 half-lives (whichever is longer)
  - **IL-6-inhibitors** shall not have been given within 6 weeks or 5 half-lives (whichever is longer)
    - Note: Tocilizumab is allowed as a rescue therapy after study start.
- Use of **high-dose corticosteroids** equivalent to >20mg of prednisolone daily for more than 14 days a month before study inclusion.
- Received dexamethasone 6mg once daily for COVID-19 for more than 4 days
- **Had symptomatic COVID-19 for more than 14 days, or was admitted to hospital for more than 7 days**.
  - Note: The patients can be included if they have been hospitalised early in the disease and then progressing after > 7 days of hospitalisation, if symptoms have been present for < 14 days.

Exclusion Criteria

- Use of strong inhibitors of organic anion transporter 3 (OAT3; eg. probenecid) that cannot be discontinued.
- Received neutralising antibodies against COVID-19
- Received live vaccine in the past 4 weeks before screening, or plans to have live vaccine in the next 90 days.
- Use of extracorporeal blood purification to remove proinflammatory cytokines
- Known active or latent tuberculosis treated for less than 4 weeks with adequate medication (screening is not required)
- **Suspected serious infection** (aside from COVID-19), where the study doctor believes the use of baricitinib will be a risk.
- **Active cancer**, where the study doctor believes it will be a risk to take baricitinib.

Exclusion Criteria

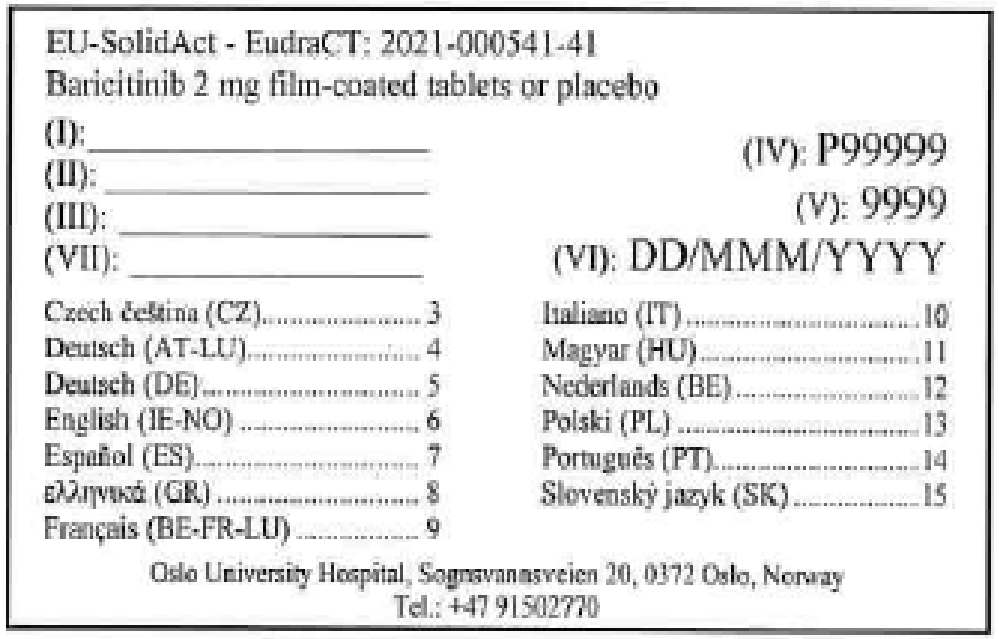
- **Thromboembolism** (DVT or LE) in the past 12 weeks or earlier if recurrent
- **Neutropenia** (neutrophilic granulocytes <1,0 × 10^9/L)
- **Lymphopenia** (lymphocytes <0,2 × 10^9/L)
- **ALAT or ASAT** > 5 times upper limit of normal.
- **Kidney failure** corresponding to GFR <15 ml/min/1,73^2
  - Patients with GFR 15-30 ml/min/1.73^2 are excluded unless potential benefint outweighs potential risk.
- Known hypersensitivity to baricitinib.
- **Pregnancy or lactation**, or planning to become pregnant during the study period.
  - Women of child-bearing age must take a pregnancy test before study start. They must agree to use highly effective contraception or abstinance for at least 1 week.
- **Participation in another study** for immune modulating treatment of COVID-19.

Medications/drug handling

Baricitinib 2 mg tablets or placebo tablets

- Film-coated
- 4 mg (two tablets) once daily while hospitalized or ≤ 14 days
- PO or by NG-tube
- with or without food
- dose adjustments due to drug interactions and renal function
- 1 bottle per patient

Booklet Label

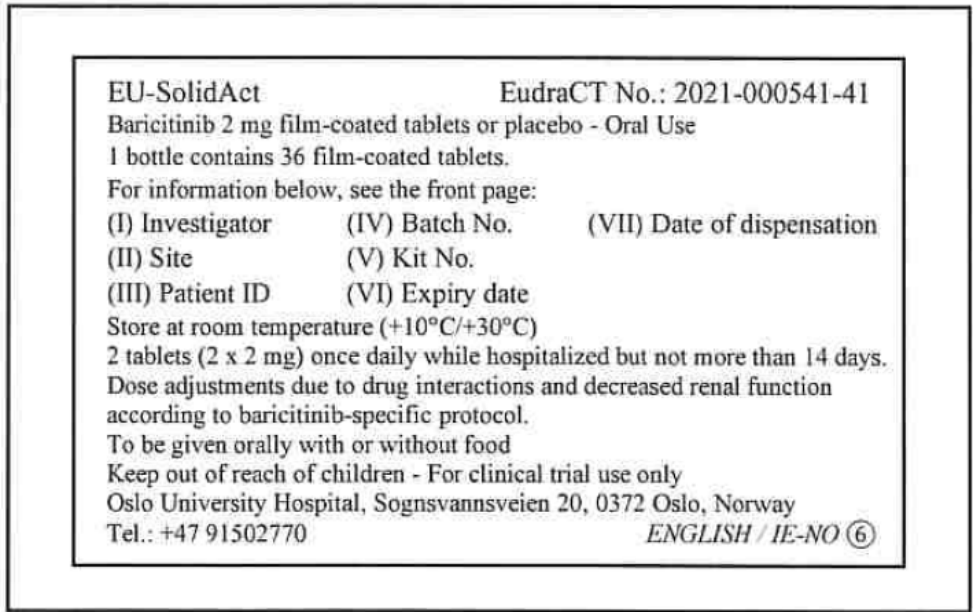

EU-SolidAct - EudraCT: 2021-000541-41
Baricitinib 2 mg film-coated tablets or placebo

(I): _____
(II): _____
(III): _____
(VII): _____

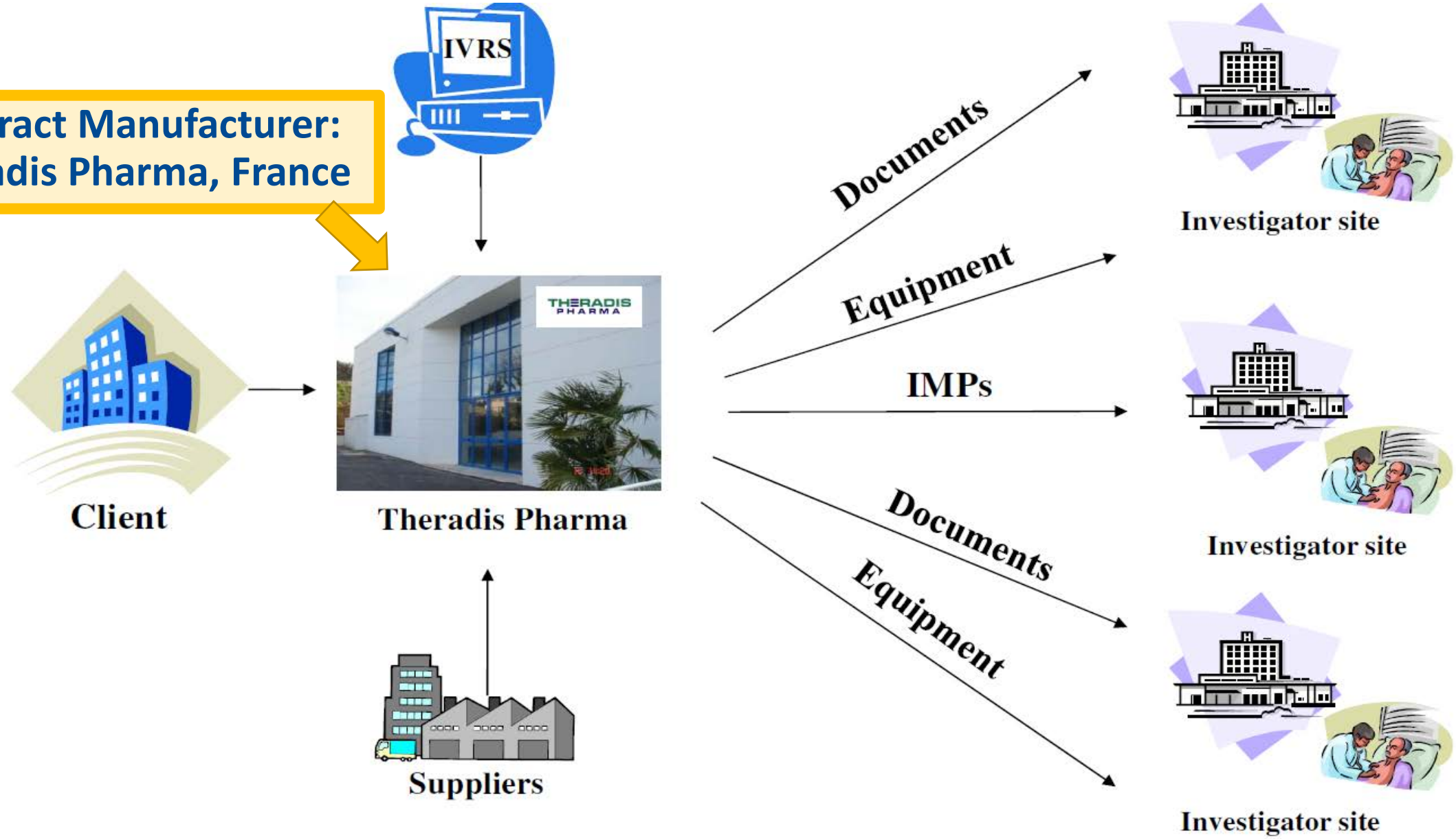
(IV): P99999
(V): 9999
(VI): DD/MMM/YYYY

Czech čeština (CZ) 3
Deutsch (AT-LU) 4
Deutsch (DE) 5
English (IE-NO) 6
Español (ES) 7
ελληνικά (GR) 8
Français (BE-FR-LU) 9
Italiano (IT) 10
Magyar (HU) 11
Nederlands (BE) 12
Polski (PL) 13
Português (PT) 14
Slovenský jazyk (SK) 15

Oslo University Hospital, Sognsvannsveien 20, 0372 Oslo, Norway
Tel.: +47 91502770


EU-SolidAct EudraCT No.: 2021-000541-41
Baricitinib 2 mg film-coated tablets or placebo - Oral Use
1 bottle contains 36 film-coated tablets.
For information below, see the front page:
(I) Investigator (IV) Batch No. (VII) Date of dispensation
(II) Site (V) Kit No.
(III) Patient ID (VI) Expiry date
Store at room temperature (+10°C/+30°C)
2 tablets (2 x 2 mg) once daily while hospitalized but not more than 14 days.
Dose adjustments due to drug interactions and decreased renal function according to baricitinib-specific protocol.
To be given orally with or without food
Keep out of reach of children - For clinical trial use only
Oslo University Hospital, Sognsvannsveien 20, 0372 Oslo, Norway
Tel.: +47 91502770 *ENGLISH / IE-NO* ⑥

Contract Manufacturer: Theradis Pharma, France



Drug Distribution

- Initial supply: 10 bottles to each site
- **Acknowledgement of receipt:** Send to solidact@theradispharma.com within 24 h of reception
- Shipped with **temperature logger** and delivery note
- **Download the T◦ readings** for each delivery and send to solidact@theradispharma.com within 24 h of reception

Deviations/complaints

- Report any **anomaly** (deviations) for instance temperature variations, damaged products, lost products to solidact@theradispharma.com and solidact@ous-hf.no as soon as possible and within 24 hours

- Report any product **complaints** to solidact@ous-hf.no as soon as possible and within 24 hours

- **Emergency: (e.g. product complaints which can lead to recall) call tel. +47 91502770 ASAP (OUH switchboard)**

Storage/Drug Accountability (ISF section 7)

- **Use NORCRIN SOP LM 2.13 + templates**
- LM 2.13.2 Temperature log - monitor temperature every working day (ISF 7.5)
- LM 2.13.3 Drug Accountability Form (ISF 7.6)
- LM 2.13.6 Investigational Medicinal Product – Drug Reconciliation (ISF 7.6)
- LM 2.13.7 Destruction of Investigational Medicinal Product: **do not destroy any study drug until the monitor/sponsor has given permission** (ISF 7.7)

LEGEMIDDELREGNSKAP / DRUG ACCOUNTABILITY FORM

PROTOKOLL NUMMER PROTOCOL NUMBER

STUDIESTED/ SENTER NR SITE/CENTER NO

PRODUSENT MANUFACTURER

LOKAL UTPRØVER INVESTIGATOR AT SITE

TITTEL STUDIE PROTOCOL TITLE

OPPBEVARING STORAGE CONDITIO

Temperatur fra oC til oC, beskyttet mot lys Temperature range oC, protected from light

STUDIEMEDISIN STUDY MEDICATION

Navn, pakningsstørrelse, konsentrasjon / styrke Name, vial size, concentration / strength

LA PLAS STO E LOCATIO

MOTTAK / RECEIVED

UTLEVERING / DISPENSED

RETUR / RETURNED

DESTRUKSJON/ RETUR DESTRUCTION/ RETURN

KOMMENTAR COMMENTS

Medisin nummer Medication ID	Batch Utl.dato/ Exp date	Antall Number	Dato Date	Sign mottatt/ received	Pas nr./ initialer Patient nr/ initials	Antall Number	D Date	ert dispensed	Lager-beholdning Balance	Antall Number	Dato Date	Sign	Dato/Date Sign

Drug Accountability

Oslo University Hospital

Delivery from Pharmacy to Hospital Department

- **Signed agreement** between **Principal Investigator and pharmacy** (responsibility of the Prinicipal Investigator on behalf of sponsor)

- Study drugs to be delivered as soon as possible after reception

INSERM – IMP management through eCRF

- INSERM imports IMP files in the eCRF (= available IMP at Theradis Pharma)
- INSERM creates orders in the eCRF for IMP to be sent to a site (blocks of 10). Alert e-mail from INSERM to Theradis Pharma. Theradis Pharma sends IMPs to sites.
- **INSERM records delivery confirmations in the eCRF. Only IMP with the «Available at Investigator's» status can be allocated to a patient.**
- INSERM receives alert e-mails from eCRF when site's stock is getting low
- INSERM orders re-supplies of IMP for sites after confirmation by sponsor

Monitoring

Aim of monitoring

- Verify
  - That the rights and wellbeing of the participants are well taken care of
  - That the data collected are correct, complete and in accordance with the source data
  - That the trial is conducted in accordance with approved protocol, ICH-GCP and local laws and regulations

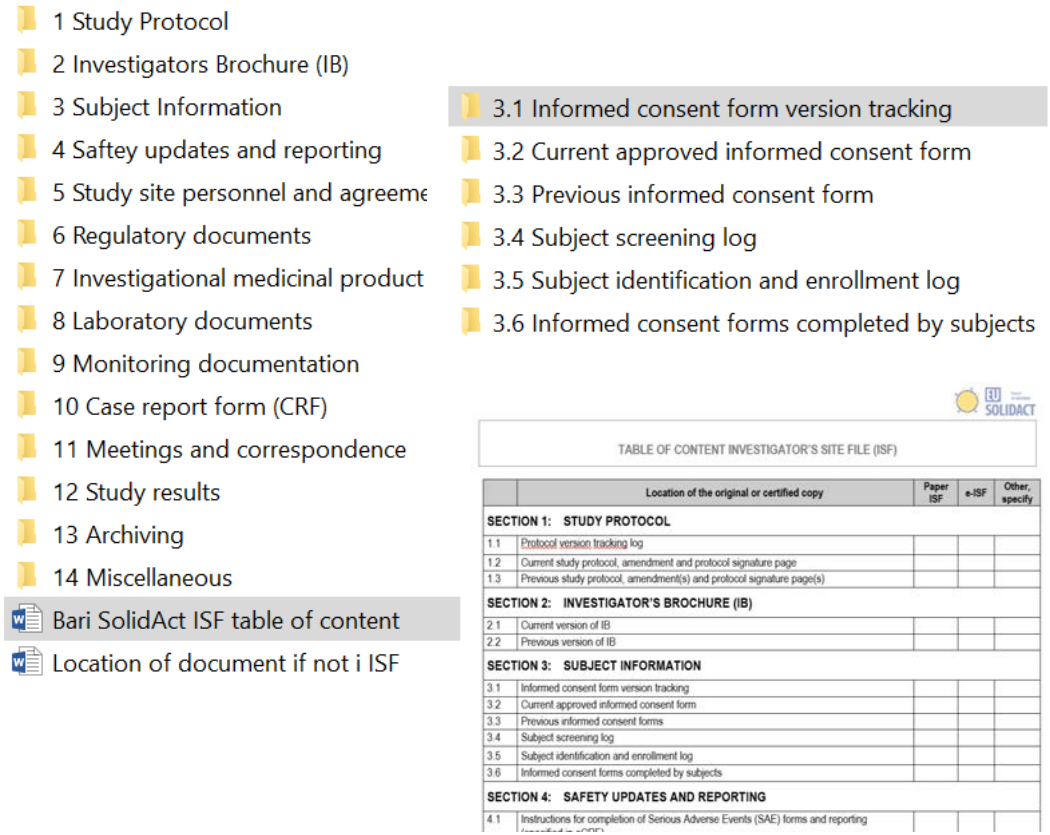
  - Monitoring is required by law for clinical drug trials

Monitoring of Bari-SolidAct

- Initiation visit **before** any patients are enrolled at your site
- First monitoring visit will take place after inclusion of 1-3 patients
- Monitoring visits **every third month** during enrollment
- Close-out visit after last patient last visit

- **On-site monitoring visits** will be performed when feasible
- Off-site / telephone / videoconference will be used as back-up

Before Initiation - ISF



- ISF is sent to you by mail, updated documents will be sent on an ongoing basis
- Contains a table of contents and many of the documents and logs required, sorted in folders
- You will have to print the documents and file them in a binder, according to the table of contents
- Complete headings with site number and investigator name where applicable
- File CVs, GCP certificates and local approval/PVO, complete the delegation log
- The monitor will check the file during the initiation and will be available for support

Initiation Visit

- The monitor will go through the initiation visit check list / report
- Special attention will be paid to
  - Documentation of source data
    - Traceability of all source data (ALCOA-principles)
    - Completed source data verification list
  - Registration and reporting of AE and SAE
    - Investigators must assess relation and severity
  - Registration and reporting of protocol deviations and serious breaches
  - Documentation of training at the site
    - Training log
    - Training in trial specific procedures / procedures not part of common patient treatment

Green Light

- If all essential documents are in place (agreements, approvals, CVs and GCP certificates), training is documented and the delegation log is complete, the monitor will give you **green light to start inclusion**
- However, you will not be able to start inclusion until you have received the study drug
- It will take up to **three working days** for you to receive study drug, when the green light document is forwarded from sponsor at OUS to INSERM and Theradis

Monitoring

- Source data verification for all patients for critical data
  - ICF date
  - Inclusion criteria GI-2 and GI-5b, and exclusion criteria SE-01, SE-02 and SE-03
  - Treatment kit number
  - Verify that all medications taken within 14 days of admission are registered in the eCRF
  - Verify that all medications given for SARS-CoV-2 during hospitalization, are registered with correct start and stop dates
  - Verify CRP, ferritin and D-dimer values at Baseline (Day 1), D8 (Day 8) and D15 (Day 15)
  - All AEs grade 3 and 4, included start and stop dates, severity and relationship to IMP, from screening to end of study / early withdrawal
  - All information at the SAE initial report (two pages) and complementary reports, as applicable from screening to end of study / early withdrawal
  - Discharge date
  - Date of early withdrawal and reason of early withdrawal, if applicable and date of death, if applicable (reason of death will be captured in the SAE form)

Monitoring

- In addition, the following will be checked
  - Essential documents / ISF binder
  - Informed consent forms
  - Endpoints (registration of the SpO_2/FiO_2-ratio)
  - Safety (routine in place for registration)
  - Protocol deviations
  - IMP (labeling, storage and accountability)
  - Facilities and equipment for biobank, if applicable

Close-Out and Reports

- After the last trial subject has completed the last visit, a close-out monitoring visit will be performed at each site
- May be combined with the last regular monitoring visit if applicable

- All reports will be written in English and sent to you within 14 calendar days after the visit
- You will have to follow up on the action items listed in **Appendix 1 Queries pending after monitoring visit**, sign off when solved and return to the monitor within the timelines given in the appendix

ICH-GCP reminder - ICFs

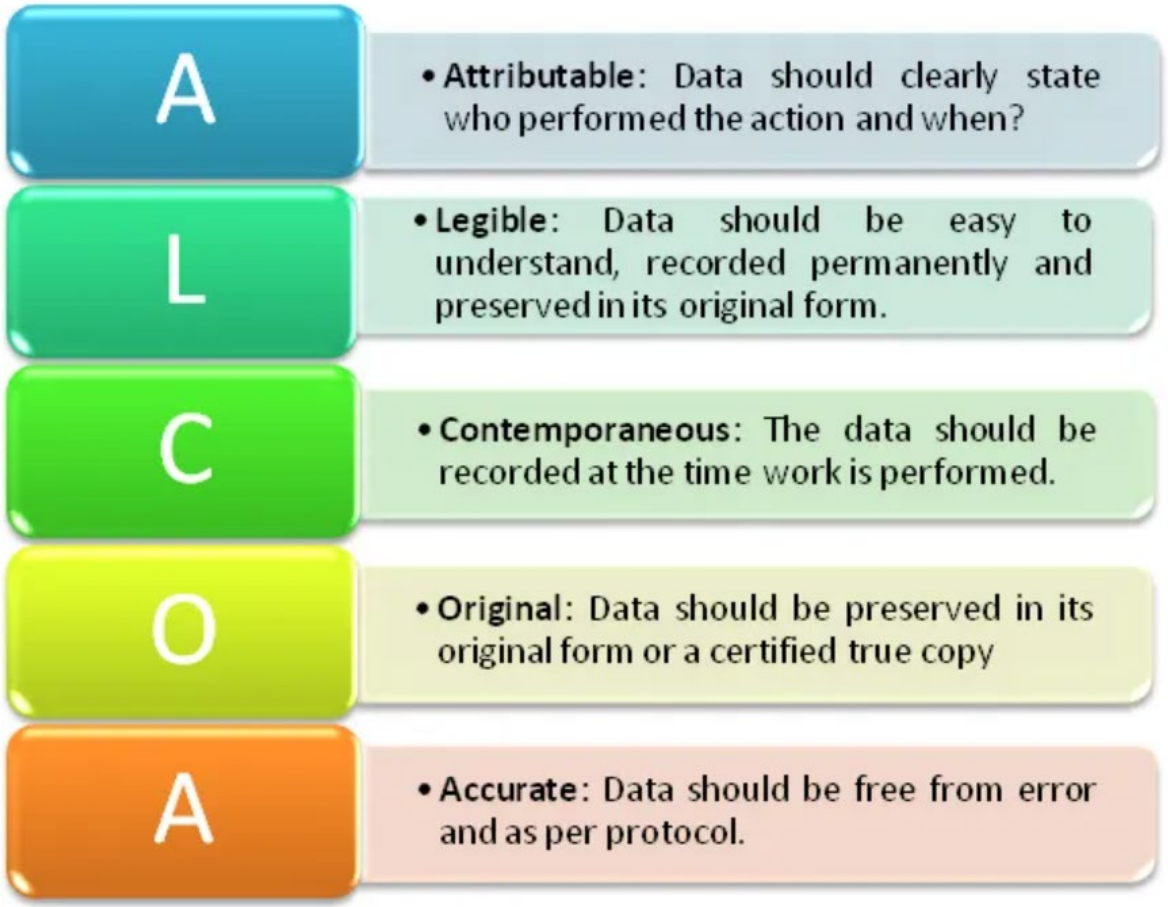
- The patients should sign and date the ICF themselves, **before** any study related procedures are performed
- The person informing the patient should sign and date **after** the patient
- The patient should have a copy of the signed ICF
- The following should be documented in the medical records:
  - Have recieved written and oral information about the trial
  - Have signed the ICF
  - Have recieved a copy

ICH-GCP reminder - AEs

- An investigator has to evaluate the
  - Severity of the event (mild, moderate, severe, life threatening)
  - Relationship to IMP (unlikely, possible, probable)
- That an investigator has done the evaluation, has to be documented
  - The investigator document relationship and severity in the patient's medical records, or
  - The investigator register information about relationship and severeity directly in the eCRF, or
  - The investigator add this information on an AE-log, and sign and date the log

ICH-GCP Reminder - Source Data

- Source data is the place where the data first is written
- Source data should always be traceable, e.g. the person who write the data, should sign and date when collecting the data, if this is not registered automatically (as in the electronical medical records)



ALCOA Principle for Data Integrity

And finally …

- The monitor is here to help you through the study, ask for advices when needed
- Remember to enter data and answer queries before each monitoring visits
- The monitor needs a place to sit, access to the ISF, and read access to the electronic medical records
- And at the end of the day; some time with the investigator and study nurse to discuss findings and issues

Brief introduction to eCRF

Inserm
Institut national
de la santé et de la recherche médicale

Oslo University Hospital

Part of EU-RESPONSE
EU SOLIDACT

Connection

- CSOnline is an Ennov clinical solution for online clinical trial management

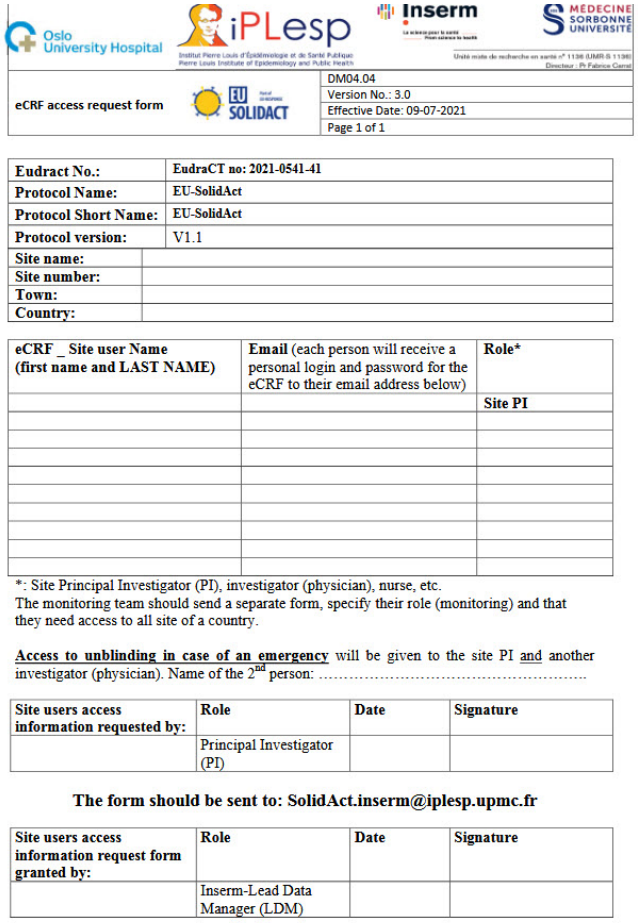
- Website address: *https://www.ccde-ecrf.com/EnnovClinical/login*

Choose the interface language

How to request access?

- A form should be signed by the PI and sent to Inserm: solidact.inserm@iplesp.upmc.fr

- You will receive an email with your personal login and password. You must log in to the eCRF at least once within 15 days of receiving the email otherwise your access will not be available anymore



Oslo University Hospital | iPLesp | Inserm | Médecine Sorbonne Université

eCRF access request form	DM04.04
	Version No.: 3.0
	Effective Date: 09-07-2021
	Page 1 of 1

Eudract No.:	**EudraCT no: 2021-0541-41**
Protocol Name:	**EU-SolidAct**
Protocol Short Name:	**EU-SolidAct**
Protocol version:	V1.1
Site name:	
Site number:	
Town:	
Country:	

eCRF _ Site user Name (first name and LAST NAME)	**Email** (each person will receive a personal login and password for the eCRF to their email address below)	**Role***
		Site PI

*: Site Principal Investigator (PI), investigator (physician), nurse, etc.
The monitoring team should send a separate form, specify their role (monitoring) and that they need access to all site of a country.

Access to unblinding in case of an emergency will be given to the site PI and another investigator (physician). Name of the 2nd person: .....

Site users access information requested by:	**Role**	**Date**	**Signature**
	Principal Investigator (PI)		

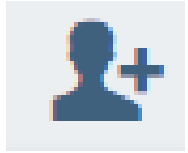
The form should be sent to: SolidAct.inserm@iplesp.upmc.fr

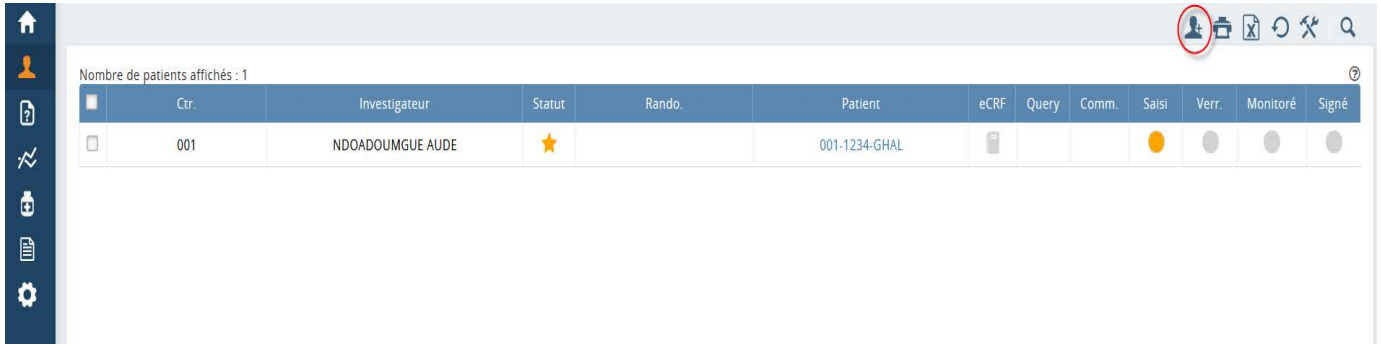
Site users access information request form granted by:	**Role**	**Date**	**Signature**
	Inserm-Lead Data Manager (LDM)		

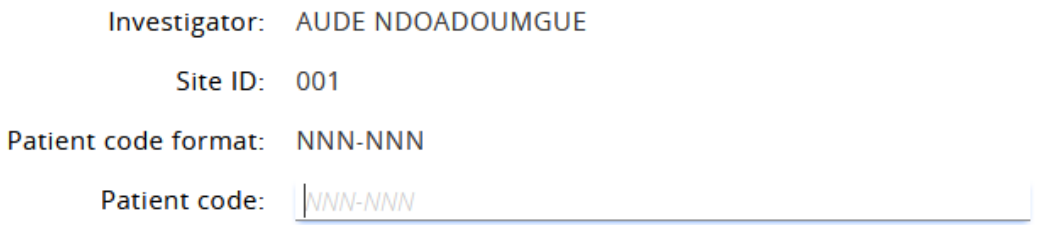
Creating a patient

Patients are created by clicking the “patient overview” section.

Click on the "Create a new patient" button:





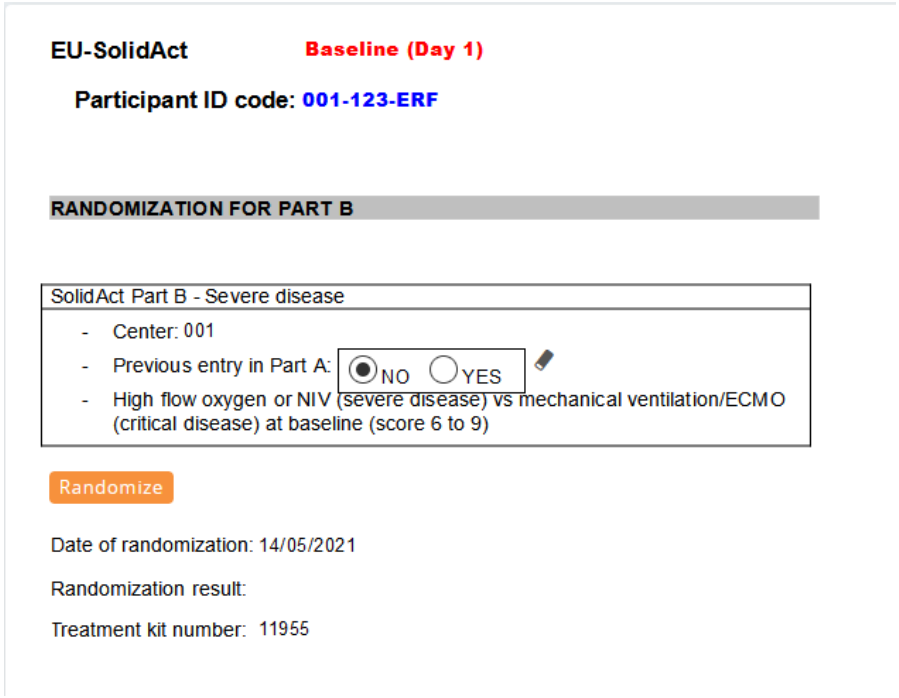


Patient ID code

NNN = center n°

NNN = patient n°

Randomization


EU-SolidAct Baseline (Day 1)

Participant ID code: 001-123-ERF

RANDOMIZATION FOR PART B

SolidAct Part B - Severe disease

- Center: 001
- Previous entry in Part A: ◉ NO ○ YES
- High flow oxygen or NIV (severe disease) vs mechanical ventilation/ECMO (critical disease) at baseline (score 6 to 9)

Randomize

Date of randomization: 14/05/2021

Randomization result:

Treatment kit number: 11955

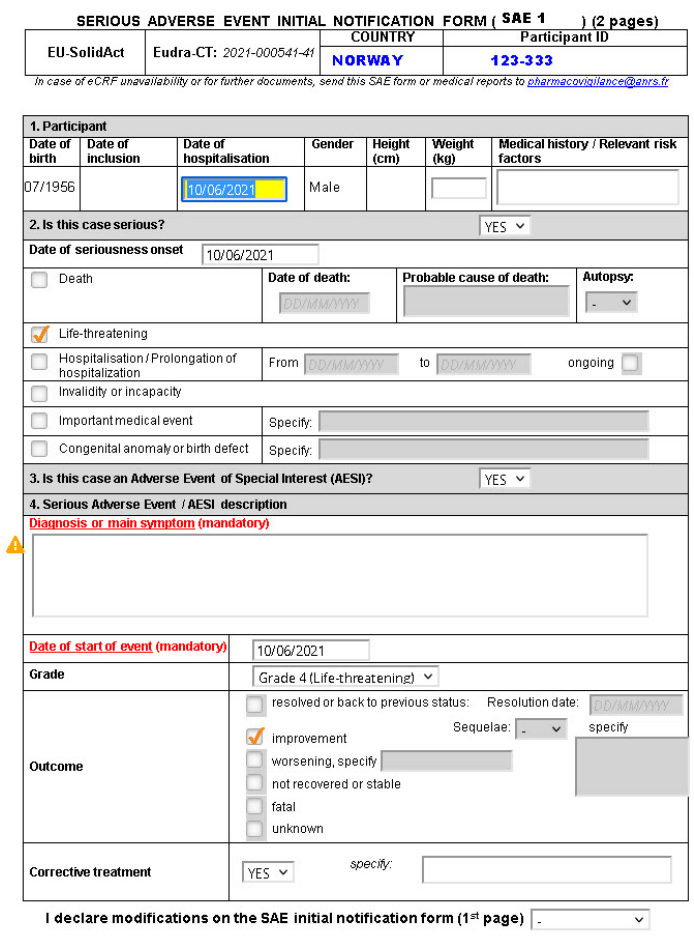
- Baseline visit
- Specify if previously included in Part A of the study and click on the Randomize button
- Minimum information needed to allow randomization:

1) Consent page
2) Clinical status / WHO Disease Stage at screening

} Consent and study selection

3) Study treatment arm available at the centre (Page 1)
4) Inclusion and exclusion criteria (Pages 2-4)
5) WHO COVID-19 Disease progression scale at baseline (Page 12)

SAE notification (initial notification)



SERIOUS ADVERSE EVENT INITIAL NOTIFICATION FORM (SAE 1) (2 pages)

EU-SolidAct	Eudra-CT: 2021-000541-41	COUNTRY	Participant ID
		NORWAY	123-333

In case of eCRF unavailability or for further documents, send this SAE form or medical reports to pharmacovigilance@anrs.fr

1. Participant

Date of birth	Date of inclusion	Date of hospitalisation	Gender	Height (cm)	Weight (kg)	Medical history / Relevant risk factors
07/1956		10/06/2021	Male			

2. Is this case serious? YES

Date of seriousness onset: 10/06/2021

- Death — Date of death: DD/MM/YYYY — Probable cause of death: — Autopsy: -
- Life-threatening
- Hospitalisation / Prolongation of hospitalization — From DD/MM/YYYY to DD/MM/YYYY ongoing
- Invalidity or incapacity
- Important medical event — Specify:
- Congenital anomaly or birth defect — Specify:

3. Is this case an Adverse Event of Special Interest (AESI)? YES

4. Serious Adverse Event / AESI description

Diagnosis or main symptom (mandatory)

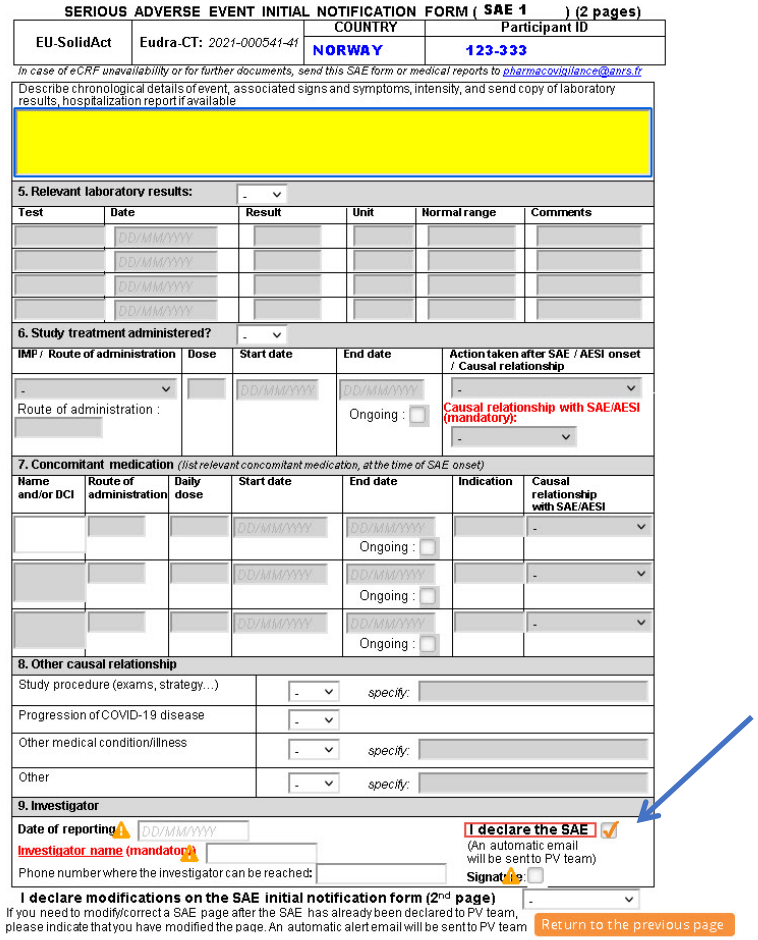
Date of start of event (mandatory): 10/06/2021

Grade: Grade 4 (Life-threatening)

Outcome:
- resolved or back to previous status: Resolution date: DD/MM/YYYY
- Sequelae: - specify
- improvement
- worsening, specify
- not recovered or stable
- fatal
- unknown

Corrective treatment: YES specify:

I declare modifications on the SAE initial notification form (1st page) -



SERIOUS ADVERSE EVENT INITIAL NOTIFICATION FORM (SAE 1) (2 pages)

EU-SolidAct	Eudra-CT: 2021-000541-41	COUNTRY	Participant ID
		NORWAY	123-333

In case of eCRF unavailability or for further documents, send this SAE form or medical reports to pharmacovigilance@anrs.fr

Describe chronological details of event, associated signs and symptoms, intensity, and send copy of laboratory results, hospitalization report if available

5. Relevant laboratory results: -

Test	Date	Result	Unit	Normal range	Comments
	DD/MM/YYYY				
	DD/MM/YYYY				
	DD/MM/YYYY				
	DD/MM/YYYY				

6. Study treatment administered? -

IMP / Route of administration	Dose	Start date	End date	Action taken after SAE / AESI onset / Causal relationship
- Route of administration :		DD/MM/YYYY	DD/MM/YYYY Ongoing :	- Causal relationship with SAE/AESI (mandatory): -

7. Concomitant medication *(list relevant concomitant medication, at the time of SAE onset)*

Name and/or DCI	Route of administration	Daily dose	Start date	End date	Indication	Causal relationship with SAE/AESI
			DD/MM/YYYY	DD/MM/YYYY Ongoing :		-
			DD/MM/YYYY	DD/MM/YYYY Ongoing :		-
			DD/MM/YYYY	DD/MM/YYYY Ongoing :		-

8. Other causal relationship

Study procedure (exams, strategy…)	-	specify:
Progression of COVID-19 disease	-	
Other medical condition/illness	-	specify:
Other	-	specify:

9. Investigator

Date of reporting DD/MM/YYYY

Investigator name (mandatory)

Phone number where the investigator can be reached:

I declare the SAE ☑ (An automatic email will be sent to PV team)

Signature:

I declare modifications on the SAE initial notification form (2nd page) -

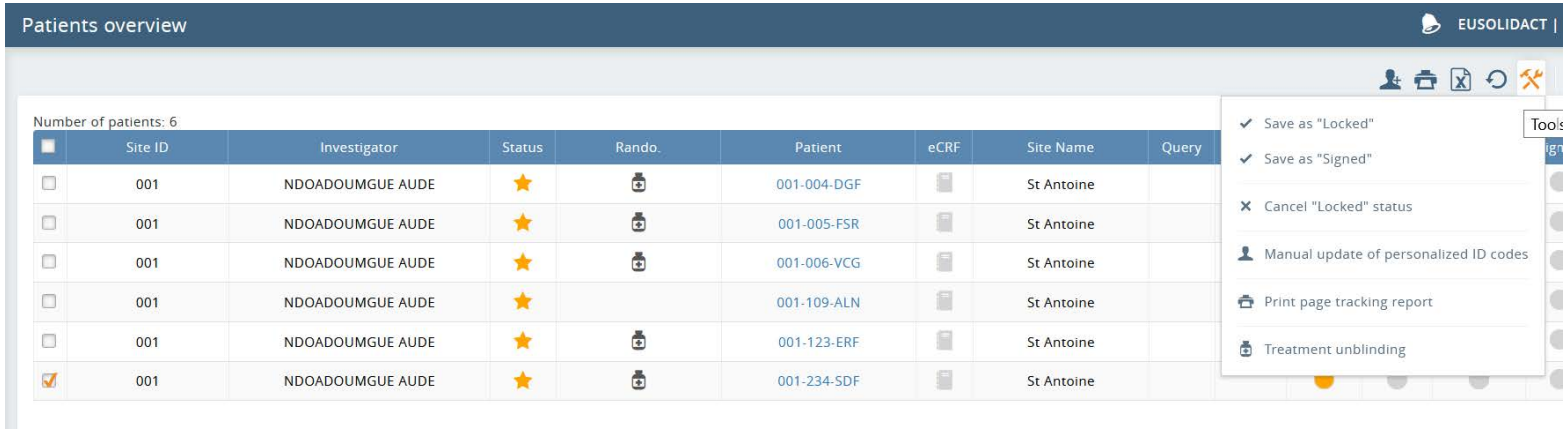
If you need to modify/correct a SAE page after the SAE has already been declared to PV team, please indicate that you have modified the page. An automatic alert email will be sent to PV team

Return to the previous page

An automatic email alert will be sent to the pharmacovigilance team

Unblinding

- Two persons in each site will have access to unblinding with their personal login and password
- Should be done only if required for the participant's safety
- Select the patient to be unblinded and click on the "Tools" icon in the patient overview page
- Select "Treatment unblinding" and choose the randomization to be unblinded
- Enter again your password, the patient ID and the reason for Unblinding
- Unblinding result will be displayed



PROM

- Inserm will send to the PI of each site an excel file associating each participant ID code to a PROM link:

	A	B	C	D	E	F	G	H	I	J	K	L
1	**Patient ID code**	**Link to the PROM questionnaire**										
2	001-001	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=QAK-EFJ&language=en										
3	001-002	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=EHY-WHJ&language=en										
4	001-003	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=ZUN-LKJ&language=en										
5	001-004	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=ZGV-GZV&language=en										
6	001-005	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=XLP-CZY&language=en										
7	001-006	https://eu5se.voxco.com/SE/?st=GWjo7z7TmGxNRA2V%2B1dkNxGt5%2Fdl2Sa9smAxasvqSz4%3D&ANONYMAT=RFZ-NXY&language=en										
8												
9												

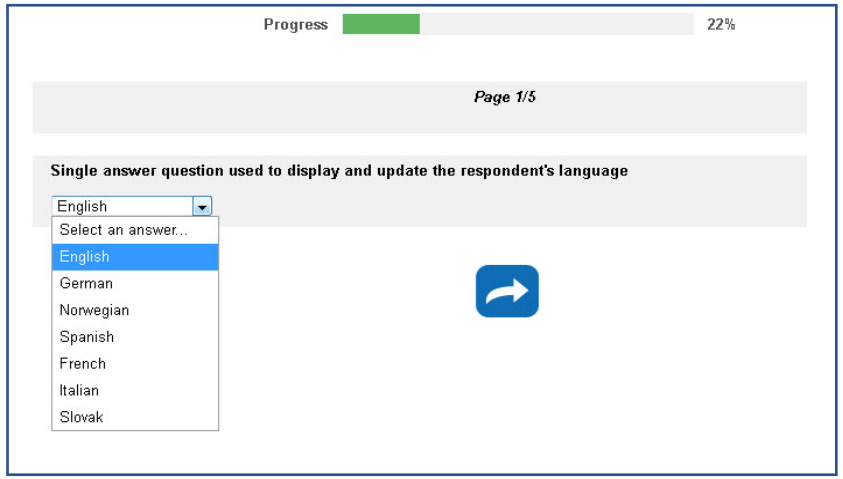
- The excel file is also available in the “document” section of the eCRF (password)

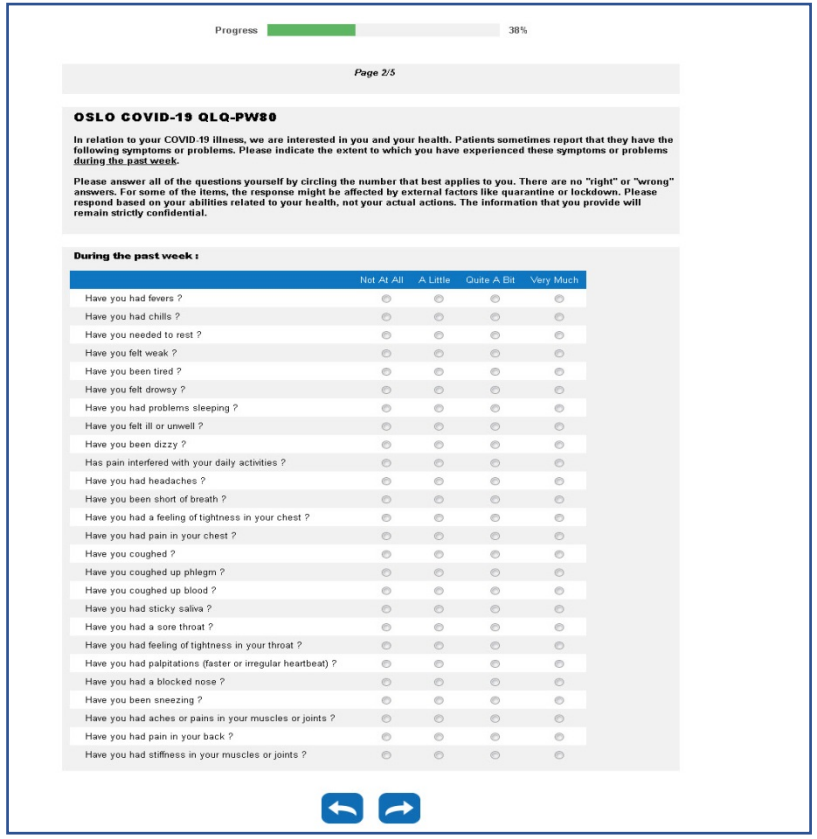
- Make sure **not** to click on a PROM questionnaire and open it before it is required to fill it

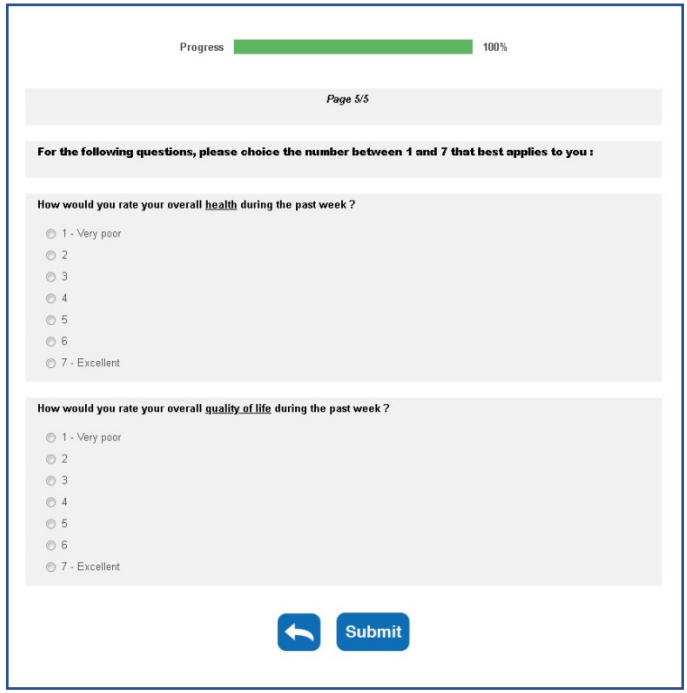
- When a patient reaches **D91 visit**, a health care professional sends the link to the questionnaire by email, SMS/text message or both, to the patient and calls him/her to check that they received and completed the questionnaire.

PROM

- The PROM questionnaire is made of 5 pages







Questions?

- https://eu-response.eu/eu-solidact/