# ACUTE-PHASE TREATMENT

Coordinadores:
Joan Martí-Fàbregas - Natalia Pérez de la Ossa

RICORS-ICTUS | Instituto de Salud Carlos III

# Workpackages

**WP1:** Improvement of reperfusion rates and patient selection

**WP2:** Improvement of the benefit/risk balance for iv thrombolysis and mechanical thrombectomy

**WP3:** Management of acute intracerebral hemorrhage and acute subarachnoid hemorrhage

**WP4:** Prevention and management of complications during acute stroke

# Workpackages

**WP1:** Improvement of reperfusion rates and patient selection

**SMS-P (Spanish Minor Stroke Perfusion)**
**COLLATERALS in automated perfusion CT**
**VESTA STUDY (imaging in long time window)**

**WP2:** Improvement of the benefit/risk balance for iv thrombolysis and mechanical thrombectomy

**HOPE TRIAL (Hemodynamic Optimization after MT)**
**MORPHEUS REGISTRY (Anesthesia in posterior stroke with MT)**
**CHOICE-2 TRIAL (intra-arterial rt-PA add-on to MT)**

**WP3:** Management of acute intracerebral hemorrhage and acute subarachnoid hemorrhage

**ICH-SCORE (Functional recovery predictive scale)**
**EPICA, EPICAS, GENVADER (Genome-wide and Epigenetic Changes associated with brain Aneurysms amd aSAH complications)**

**WP4:** Prevention and management of complications during acute stroke

**INGLES_MC (Groin complications)**
**ELITE-SAP (Stroke-associated Pneumonia)**

# Spanish Minor Stroke Perfusion Initiative:

## SMS-P Iniciative

**IP:**
**Francisco Purroy** H.U. Arnau de Vilanova
**Manuel G. Choco** H.U. M. Broggi

**Project status**: recruitment of centers, pending aprroval from ethics committees

**Centers interested in the study**:

1. H Arnau de Vilanova , Lleida
2. H Broggi, Barcelona
3. H de la Fe, Valencia
4. La Princesa, Madrid
5. Son Espases, Palma Mallorca
6. Puerta de Hierro, Madrid
7. Sant Pau, Barcelona
8. Josep Trueta, Girona
9. Mar, Barcelona
10. Verge de la Cinta, Tortosa
11. Albacete

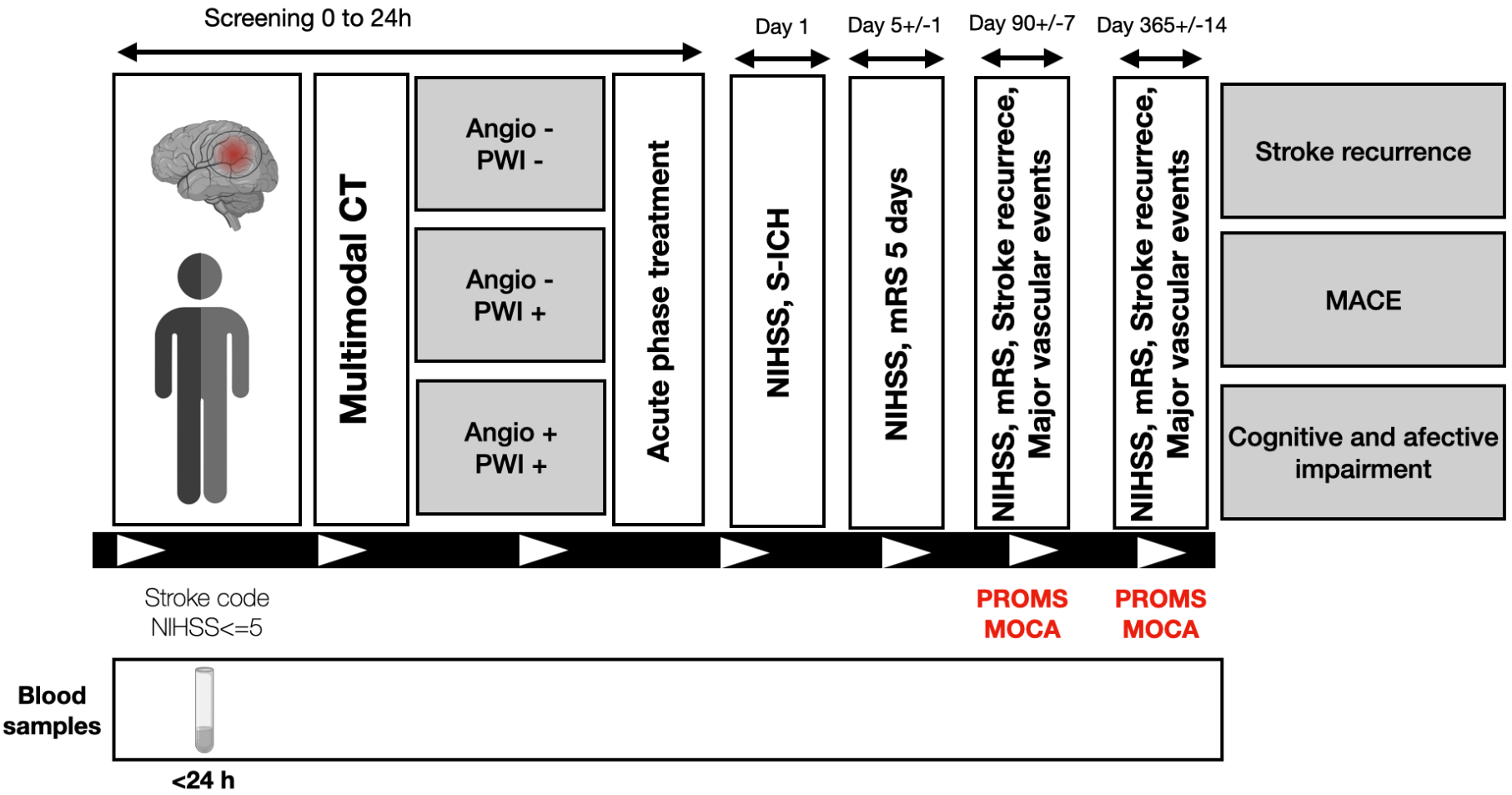
SMS-P

# Hypothesis

- The **use of multiparametric CT** (CT perfusion and CT angiography) during the acute phase of a **minor stroke** provides **additional prognostic information** on the **neurological evolution** of patients treated as stroke codes.
- This information is valuable for **therapeutic decision-making** in the acute phase and for assessing the **risk of stroke recurrence**.
- Additionally, **omic data, cfDNA and inflammatory markers** at the time of initial patient care, can be correlated with radiological information and patient prognosis both during the acute phase and follow-up.
- This approach will help identify **biomarkers for intracranial large vessel occlusion, perfusion deficits, early neurological deterioration, stroke recurrence and cognitive/afective impairment**.

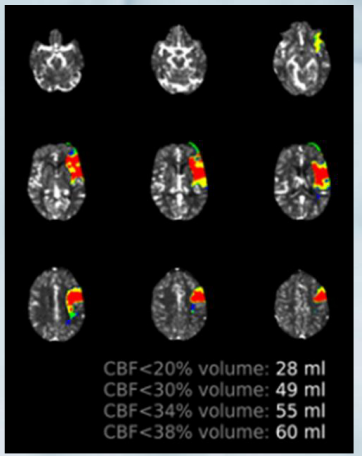
**N=814**

# SMS-P


Screening 0 to 24h
Day 1
Day 5+/-1
Day 90+/-7
Day 365+/-14
Multimodal CT
Angio - PWI -
Angio - PWI +
Angio + PWI +
Acute phase treatment
NIHSS, S-ICH
NIHSS, mRS 5 days
NIHSS, mRS, Stroke recurrece, Major vascular events
NIHSS, mRS, Stroke recurrece, Major vascular events
Stroke recurrence
MACE
Cognitive and afective impairment
Stroke code
NIHSS<=5
PROMS
MOCA
PROMS
MOCA
Blood samples
<24 h

# Study of leptomeningeal collateral circulation using automated CT perfusion software in thrombectomy-treated patients with MCA occlusion: predictive capacity for hemorrhagic transformation, therapeutic futility, and associated factors.

PROMOTOR: Hospital Universitario La Princesa (Madrid)
IP: José Vivanc
Responsable Santiago Trillo




Brain collateRals rapiD IndEx ( BIRDIE)

RAPIDAI.

Rapid CTP

Advanced CT Perfusion Analysis in Minutes

Rapid CTP is the only clinically validated software with an FDA indication to aid in the selection of patients for acute stroke therapy.

1. H.U. La Princesa (Madrid)
2. Hospital Central de Asturias (Oviedo)
3. Hospital Clínic (Barcelona)
4. CHU de A Coruña (A Coruña)
5. Hospital Josep Trueta (Girona)
6. Hospital 12 de Octubre (Madrid)
7. Hospital Ramón y Cajal. (Madrid)

# Study of leptomeningeal collateral circulation using automated CT perfusion software in thrombectomy-treated patients with MCA occlusion: predictive capacity for hemorrhagic transformation, therapeutic futility, and associated factors.

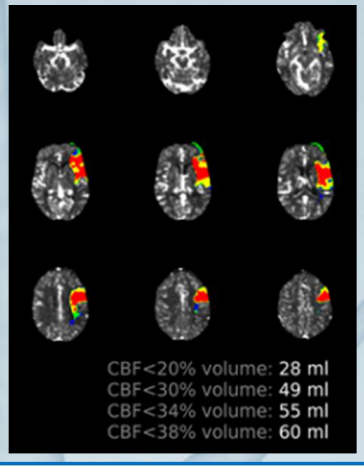
IP: José Vivancos
Responsable Santiago Trillo

We studied the ability of **automated perfusion CT software** to estimate **collateral circulation in patients treated with thrombectomy.**

We identified perfusión CT index for colateral circulation estimation (**BIRDIE index**).

Additionally, we developed tools to predict:

1) **The risk of hemorrhagic transformation**
2) **Therapeutic futility in terminal carotid occlusion**
3) **Factors that predict colateral circulation in out-of-hospital settings**




BraIn collateRals rapiD IndEx ( BIRDIE)

# PREDICTION OF HEMORRHAGIC TRANSFORMATION AFTER ENDOVASCULAR TREATMENT

Objective: To develop a predictive scale for hemorrhagic transformation (PH2) based on clinical, biochemical, and advanced neuroimaging factors.

Methods: A retrospective multicenter study of consecutive patients with M1 MCA segment or T occlusion treated with MT between 2021 and 2023 at 7 stroke centers in the RICORS-ICTUS network, with available RAPID® data **(N=1071 patients)**

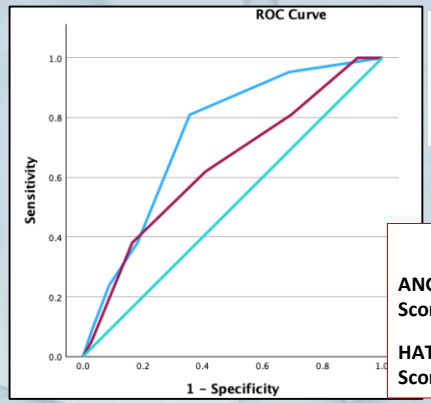
**N=1701 patients**
**48 (4,5%) hemorrhagic transformation PH2**

*Análisis multivariante*

| | OR | p |
|---|---|---|
| **Glu >200mg/dL** | 8,8 | <0,001 |
| **Leucos >15.000** | 4,2 | 0,02 |
| **Tmáx>6s >180** | 3,5 | 0,02 |
| **CBV<34% >60mL** | 2,6 | 0,01 |

***Escala ANGEL***

| | | |
|---|---|---|
| **Glucemia Urg** | >200 ó DM | 2 |
| | 0-200 | 1 |
| **Leucocitos Urg** | >15000 | 2 |
| | 0-15000 | 1 |
| **T Máx>6s** | >180 | 3 |
| | 120-180 | 2 |
| | <120 | 1 |
| **CBV<34%** | >60 | 3 |
| | 40-60 | 2 |
| | >40 | 1 |




**Source of the Curve**
ANGEL_SCORE
HATSCORE
Reference Line

| | AUC ROC | p |
|---|---|---|
| **ANGEL-Score** | **0,74** (0,64 - 0,83) | <0,01 |
| **HAT-Score** | **0,64** (0,51 - 0,76) | 0,02 |

The ANGEL scale significantly, practically, and non-invasively identified subjects at risk of PH2 prior to MT, with a better AUC than other predictive scales such as HAT

# FUTILITY OF ENDOVASCULAR TREATMENT IN TERMINAL CAROTID OCCLUSION

Objective: To predict poor outcomes after ET using a tool based on automated CT perfusion software parameters.

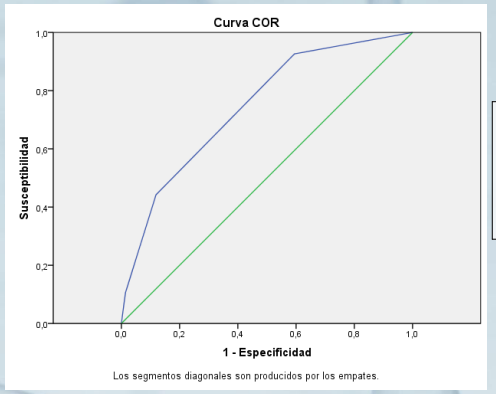
Methods: Retrospective multicenter study of consecutive patients with terminal carotid occlusion treated with MT between 2021 and 2023 at 7 stroke centers in the RICORS-ICTUS network, with available RAPID® data **(N=248 patients)**

*Análisis univariante*

| | OR | IC 95% | p |
|---|---|---|---|
| Edad > 80 años | 3,508 | 2,038-6,040 | <0,001 |
| mRS basal > 1 | 2,135 | 1,162-3,923 | 0,0015 |
| ASPECTS basal < 6 | 2,302 | 1,158-4,576 | 0,017 |
| Hipodensidad moderada-grave > 215 mL | 2,914 | 1,711-4,961 | <0,001 |
| BIRDIE < 75% | 3,459 | 1,978-6,050 | <0,001 |

*Análisis multivariante*

| | OR | IC 95% | p |
|---|---|---|---|
| **Edad > 80 años** | **4,826** | **2,612-8,916** | **<0,001** |
| **BIRDIE < 75%** | **4,830** | **2,586-9,034** | **<0,001** |




**AUC ROC**

**0,745**
IC 95% 0,683 - 0,808

P <0,01

Good prediction of futility after ET in stroke due to terminal carotid occlusion using parameters from automated software alongside other factors.

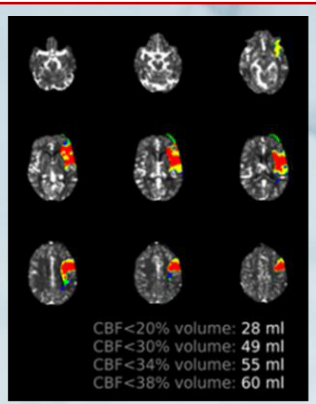
# FACTORS INFLUENCING COLLATERAL CIRCULATION

Objective: To evaluate a collateral circulation index obtained through RAPID® software, its potential determining factors, and prognostic value.

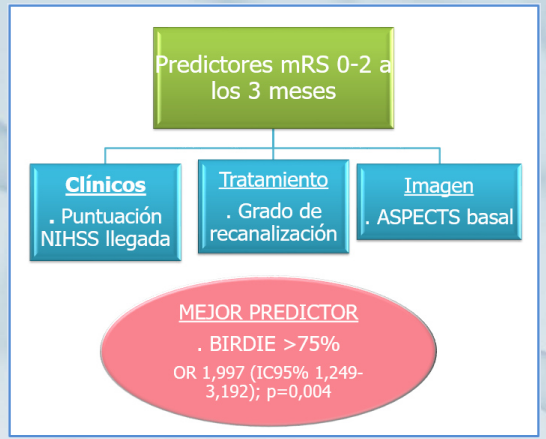
Methods: A retrospective multicenter study of consecutive patients with M1 MCA segment or T occlusion treated with MT between 2021 and 2023 at 7 stroke centers in the RICORS-ICTUS network, with available RAPID® data **(n=1074 patients)**

## Brain collateRals rapiD IndEx (BIRDIE)

$$1 - \frac{\text{Volumen con CBF<30\%}}{\text{Volumen total territorio ACM}}$$




## BIRDIE index: associated to clinical outcome




## Factors associated to BIRDIE index

| Análisis univariante de **factores asociados a BIRDIE** | |
|---|---|
| **Sexo femenino** | 88,4% vs. 84,8%; p=0,002 |
| **Presión arterial diastólica (PAD) ≤90mmHg** | 90,4% vs. 85,0%; p<0,001 |
| **Oclusión de T carotidea** | 77,7% vs. 89,7%; p<0,001 |
| **NIHSS** | rho=-0,39; p<0,001 |
| **ASPECTS basal** | rho=0,43; p<0,001 |

# VESTA Study

## Stroke treatment in the extended window: optimization of the radiological selection and transfer model of

**PROMOTOR: Germans Trias i Pujol**
**IP: Maria Hernández-Pérez**

**PARTICIPATING CENTERS:**

1. **Germans Trias i Pujol, Badalona**
2. **Bellvitge, Barcelona**
3. **Clinic, Barcelona**
4. **Josep Trueta, Girona**
5. **Arnau de Vilanova, Lleida**
6. **Mar, Barcelona**
7. **Parc Taulí, Sabadell**
8. **Sant Pau, Barcelona**
9. **Joan XXIII, Tarragona**

# OBJECTIVES



1. To evaluate whether the selection of patients for EVT in the extended window is similar in terms of safety and efficacy when using simple vs advance imaging paradigm

2. To analyze the yield of non-contrast CT post-processing software for the selection of patients for EVT in the extended window

3. To analyze the pre-hospital and PSC variables in order to generate decision trees to optimize the transfer decision of stroke code patients >6h after symptoms onset

# METHODOLOGY



CICAT 2019/2021

> 18 years

Acute ischemic stroke 6-24h

mrS 0-2

NIHSS > 5

Neuroimaging (simple or advanced) <60 min hospital

Imaging evaluation by a central core-lab

Postprocessing of non-contrast CT with Methinks AI software

MiSTAR perfusion evaluation

TO COMPARE 2 GROUPS OF PATIENTS:

1. Patients receiving simple imaging paradigm
2. Patients receiving advanced imaging paradigm

TO EVALUATE THE YIELD OF THE NCCT SOFTWARE:

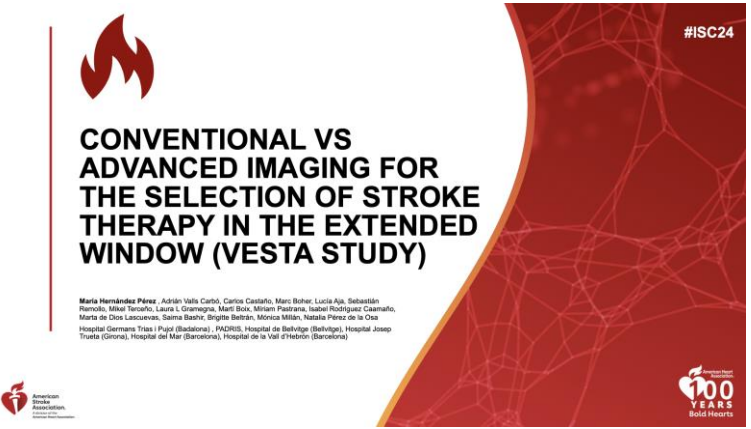
1. ¿Is the software usable/reliable?
2. ¿Is the software able to better identify patients eligible for EVT? (core or arterial occlusion identification)

DECISION TREATMENT TREES

# RESULTS



**OBJECTIVE 1**. Results presented in ISC 2024




Article writing is ongoing

**OBJECTIVE 2**. Statistical analysis done


Abstract for the ESOC 2025

**OBJECTIVE 3**

FIS requested extension

HOPE Improving cerebral perfusion after stroke

A randomized trial on **H**emodynamic **O**ptimization of cerebral **P**erfusion after **E**ndovascular therapy in patients with acute ischemic stroke (HOPE study)

Ensayo clínico PROBE (Prospective, Randomized, Open, Blinded End-point)

**Promotor: Hospital de la Santa Creu i Sant Pau**

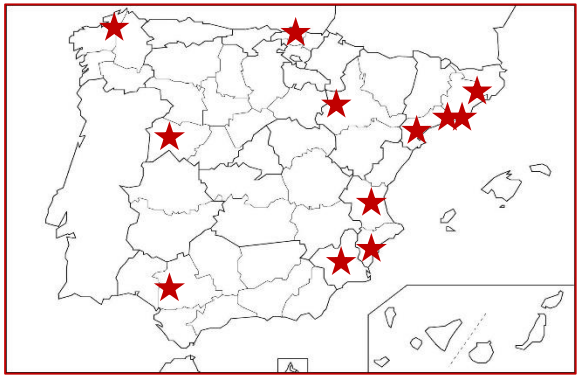
**IP: Joan Martí-Fàbregas i Pol Camps**

Financiación: Ministerio de Economía y Competitividad

(Investigación Clínica Independientes 2020)

HOSPITAL DE LA SANTA CREU I SANT PAU
FUNDACIÓ DE GESTIÓ SANITÀRIA
UNIVERSITAT AUTÒNOMA DE BARCELONA

GOBIERNO DE ESPAÑA MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD
Instituto de Salud Carlos III



**Centros participantes activados:**

1. **Hospital de la Santa Creu i Sant Pau (Barcelona)**
2. Hospital del Mar (Barcelona)
3. Hospital Josep Trueta (Girona)
4. Hospital Virgen del Rocío (Sevilla)
5. Hospital Universitario A Coruña (A Coruña)
6. Hospital Cruces (Barakaldo)
7. Hospital La Fe (Valencia)
8. Hospital Joan XXIII (Tarragona)
9. H Universitario Alicante (Alicante)
10. H Miguel Servet (Zaragoza)
11. H Virgen de la Arrixaca (Murcia)
12. Hospital de Salamanca (Salamanca)

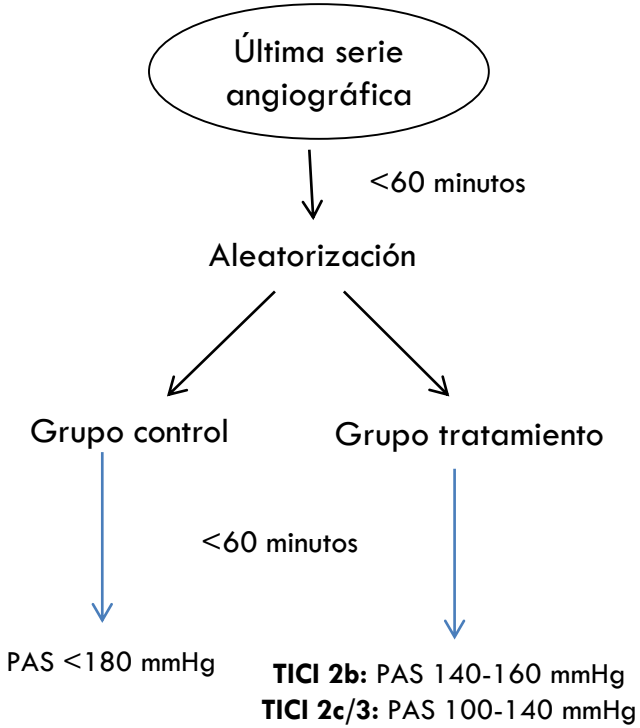
HOPE Improving cerebral perfusion after stroke

**Criterios de Inclusión**

1. Ictus isquémico <24h
2. Oclusión de gran vaso circulación anterior
3. Tratamiento endovascular
4. Recanalización exitosa (TICI ≥2b)
5. Rankin previo <3
6. Consentimiento informado

**Criterios de Exclusión**

1. ASPECTS<6
2. Oclusión distal (A2, M3-4)
3. Historia de HIC o HIC en TC basal
4. Insuficiencia cardíaca o angina inestable
5. Disección o aneurisma de aorta
6. Disección TSA, aneurisma o MAV cerebral
7. Historia de arritmias ventriculares
8. Uso de inhibidores de la MAO
9. Riesgo de ictus hemodinámico
10. Inclusión en otro ensayo clínico
11. Embarazo o lactancia



HOPE Improving cerebral perfusion after stroke

# HOPE

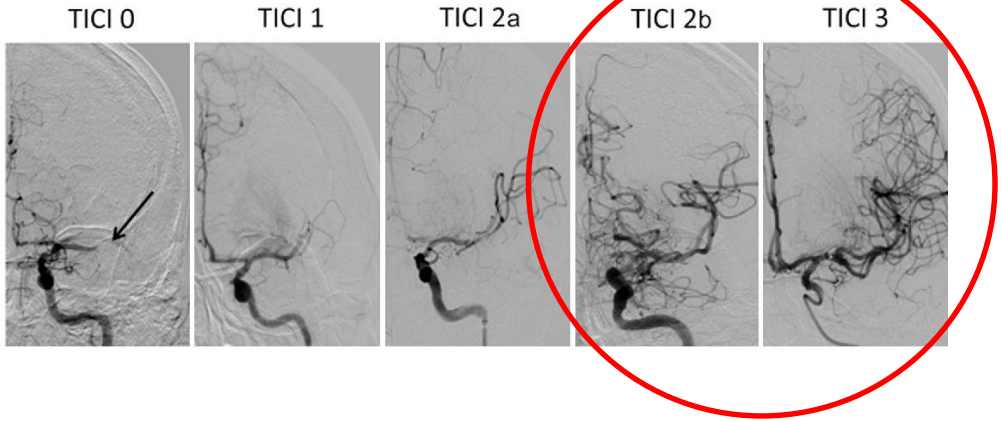
## Individualizar la presión arterial para optimizar la perfusión

Presión baja
Presión alta
→ Mal pronóstico

**Subir** la presión baja si TICI **2b**
**Bajar** la presión alta si TICI **2c-3**
→ **Buen pronóstico? mRS 3 meses**

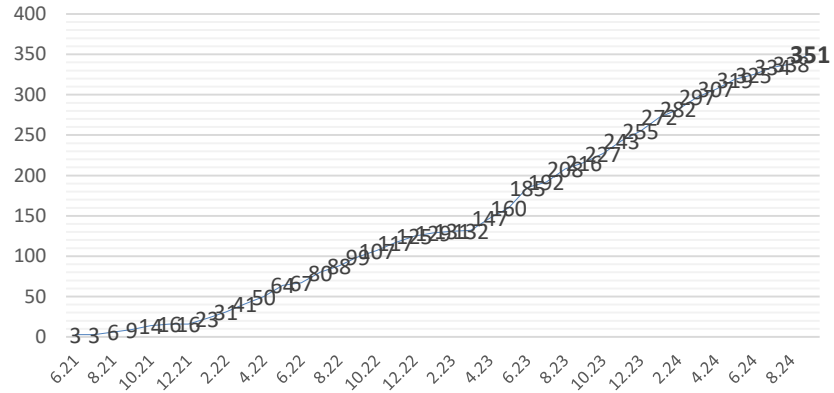
(Según TICI)

**(Menos edema**
**Menos hemorragia**
**Mejor perfusión)**



HOPE Improving cerebral perfusion after stroke

Pacientes incluidos hasta setiembre 2024




**Total sample size: 814 patients**

DSMB Interim analyses: planned at 250 and 500 patients

- Inicio inclusión • Junio 2021
- Fin inclusión • Junio 2025
- Rankin 3 meses • Setiembre 2025
- Queries • Octubre 2025
- Análisis • Noviembre 2025
- Presentación + Publicación • **ESOC. mayo 2026 ?**

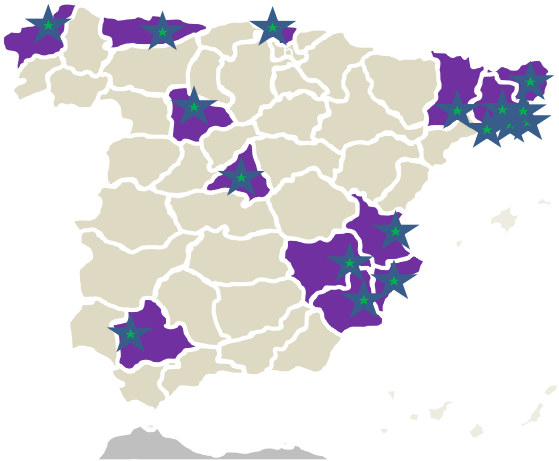
# **M**ulticentre **O**bse**R**vational study in **P**osterior mec**H**anical thromb**E**ctomy: conscio**U**s sedation vs general ane**S**thesia (MORPHEUS STROKE REGISTRY)

**PROMOTER**

Hospital Josep Trueta de Girona

**PARTICIPANTS**

1. Hospital Josep Trueta de Girona
2. Hospital Germans Trias i Pujol
3. Hospital Arnau de Vilanova
4. Hospital de Bellvitge
5. Hospital del Mar
6. Parc Taulí
7. Hospital de la Santa Creu i Sant Pau
8. Hospital Clínic de Barcelona
9. Hospital Vall d'Hebron
10. Hospital Central de Asturias
11. Hospital de Cruces
12. Hospital Clínico de Valladolid
13. Complejo Hospitalario de Albacete
14. Complejo Hospitalario de A Coruña
15. Hospital Virgen del Rocío
16. Hospital La Fe de Valencia
17. Hospital Virgen de la Arrixaca
18. Hospital General de Alicante
19. Hospital de La Princesa



# OBJECTIVES

- **Primary objective:**

- To study the association between the **type of anesthesia used during mechanical thrombectomy in patients with posterior circulation** and large vessel occlusion, and functional outcome at 3 months.

- **Secondary objectives:**

- To determine the association between **blood biomarkers** and functional outcome at 3 months (biomarker MORPHEUS study)
- To identify whether **blood pressure** during thrombectomy correlate with functional outcome at 3 months.
- To compare the effect of **the type of device** used in the mechanical thrombectomy with the degree of recanalization and functional outcome at 3 months.
- To study the effect of **fibrinolytic treatment** on the degree of recanalization and functional outcome at 3 months.

MORPHEUS STROKE Registry

# METODOLOGY

- 19 participating centers
- Prospective study: 2021-2023
- Patients with large posterior circulation vessel occlusion
- <24 hours from symptom onset
- EDC (www.morpheus-registry.com)
- **453 patients recruited**
- **Biomarker MORPHEUS study**: 6 centers

Hospital de Cruces
Hospital Clínico de Valladolid
Complejo Hospitalario de A Coruña
Hospital Virgen del Rocío
Hospital Josep Trueta de Girona
Hospital de la Santa Creu i Sant Pau

# CURRENT STATUS OF THE STUDY

- Patients recruitment and database is completed.
- No published data.
- Intermediate results were published on the Annual Meeting of the Spanish Society of Neurology (SEN) in 2023.
- Analysis of the primary objective is on-going and the publication is expected in 2025.
- Blood samples are currently being recruited and sent to the promoter center. The analysis is expected to be performed in November.

# CHemical OptImization of Cerebral Embolectomy in patients with acute stroke treated with mechanical thrombectomy 2 (CHOICE-II)

**Sponsor**: Fundació de Recerca Clínic Barcelona-IDIBAPS

**Principal Clinical Investigator:** Dr. Ángel Chamorro

**Registration Number**: NCT05797792

**EudraCT Number**: 2023-504262-32-00

**Steering Committee:**

Dr. Ángel Chamorro (chair)
Dr. Juan Arenillas
Dra. Mar Castellanos
Dra. Mª del Mar Freijo
Dra. Natalia Pérez de la Ossa
Dr. Luis San Román
Ferran Torren (statistician)

| SITE | CENTER | PRINCIPAL INVESTIGATOR |
|---|---|---|
| **1** | **H. Clinic Barcelona** | Dr. Arturo Renú |
| 2 | H. Universitario Valladolid | Dr. Juan Arenillas |
| 3 | H. Cruces | Dra. Maria del Mar Freijo |
| 4 | H. Universitario de Donostia | Dra. Patricia de la Riva |
| 5 | H. Universitario de A Coruña | Dra. Mª Dolores Fernandez |
| 6 | H. Universitario Central de Asturias | Dr. Pedro Vega |
| 7 | H. Universitario de la Fe | Dr. Lluis Morales |
| 8 | H. Germans Trias I Pujol | Dra. Laura Dorado |
| 9 | H. de la Santa Creu I Sant Pau | Dr. Pol Camps |
| 10 | H. Universitario Dr. Josep Trueta de Girona | Dr. Mikel Terceño |
| 11 | H. Universitario Virgen de la Arrixaca | Dra. Ana Morales |
| 12 | H. Universitario de Navarra | Dra. Maria Herrera |
| 13 | H. Universitario Son Espases | Dra. Raquel Delgado |
| 14 | H. Gral Universitario Dr. Balmis de Alicante | Dr. Nicolás López |

CHOICE II

**Effect of Intra-arterial Alteplase vs Placebo Following Successful Thrombectomy on Functional Outcomes in Patients With Large Vessel Occlusion Acute Ischemic Stroke**

The CHOICE Randomized Clinical Trial

Arturo Renú, MD[1,2]; Mónica Millán, MD[3]; Luis San Román, MD[4]; et al

JAMA

**QUESTION** Does the use of adjunct intra-arterial thrombolysis following an angiographically successful thrombectomy improve functional outcomes in patients with large vessel occlusion acute ischemic stroke?

**CONCLUSION** Among patients with large vessel occlusion acute ischemic stroke and successful reperfusion following thrombectomy, use of adjunct intra-arterial alteplase compared with placebo resulted in a greater likelihood of excellent neurological outcome at 90 days.

## POPULATION

61 Men
52 Women

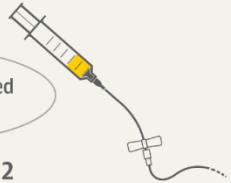
Adults with large vessel occlusion acute ischemic stroke successfully treated with thrombectomy within 24 hours of stroke onset

Mean age: 71 years

## LOCATIONS

7
Stroke centers
in Catalonia, Spain

## INTERVENTION



121 Patients randomized
113 Patients analyzed

61
**Alteplase**
Intra-arterial alteplase, 0.225 mg/kg, infused over 15 to 30 minutes

52
**Placebo**
Intra-arterial placebo infused over 15 minutes

## PRIMARY OUTCOME

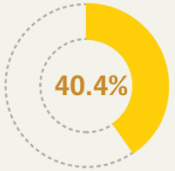
Percentage of patients with a score of 0 or 1 on themodified Rankin Scale (mRS), indicating no disability at 90 days

## FINDINGS

Patients with mRS score of 0 or 1

**Alteplase**
36 of 61 patients


**Placebo**
21 of 52 patients




The adjusted risk difference was significant:

Risk difference, **18.4%**
(95% CI, 0.3% to 36.4%; *P* = .047)



Renú A, Millán M, San Román L, et al; CHOICE Investigators. Effect of intra-arterial alteplase vs placebo following successful thrombectomy on functional outcomes in patients with large vessel occlusion acute ischemic stroke. *JAMA*. Published online February 10, 2022. doi:10.1001/jama.2022.1645

# CHOICE-II Trial

**Study Objective**:
The study objective is to validate whether the **administration of intra-arterial rt-PA is efficient as an add-on to mechanical thrombectomy** in patients with acute ischemic stroke and complete or near-complete recanalization of a proximal vessel occlusion and successful brain reperfusion on cerebral angiogram (corresponding to mTICI score 2b/3).

**Interventional Model Description:**
Multicenter, prospective, randomize, open, blinded end-point assessment **phase III Trial**.

**Masking Description:**
The evaluation of the primary outcome measure (microvascular hypoperfusion on CTP) will be conducted at the Imaging Central Core Laboratory by blinded evaluators.

The evaluation of key **clinical outcome at 3 months** will be conducted by central blinded evaluators following a structured questionnaire of the modified Rankin Scale (mRS).

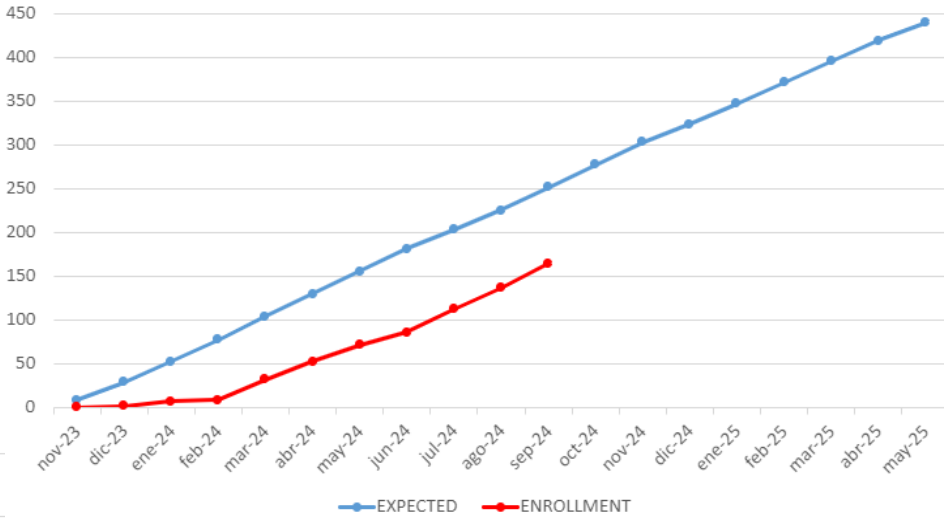
# CHOICE-II Trial

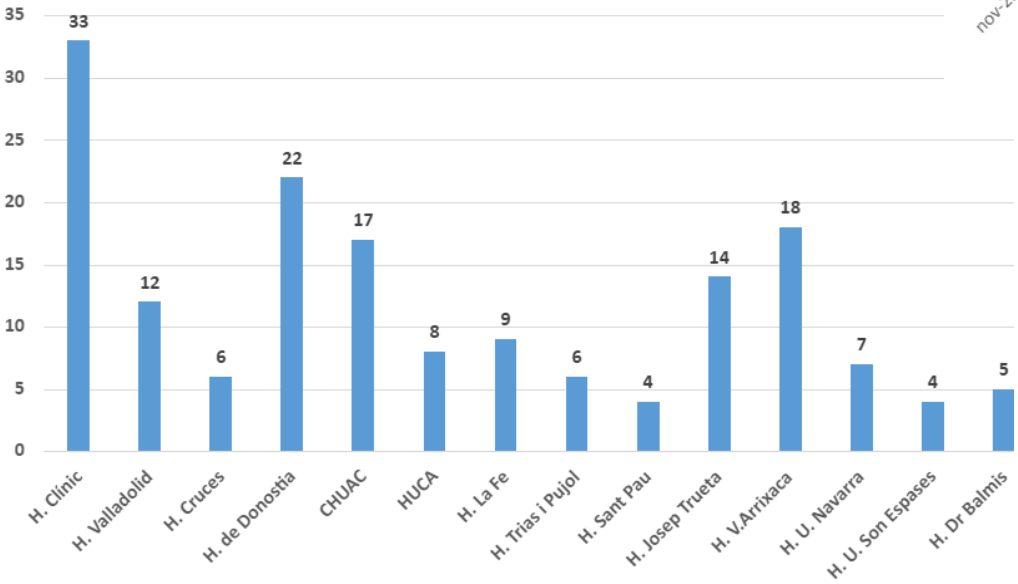
| | |
|---|---|
| **PRIMARY OUTCOME** | Microvascular hypoperfusion on brain CT Perfusion on CTPerfusion at 36±24hours post MT |
| **SECUNDARY OUTCOME** | 1.- Modified Rankin Scale (mRS) score 0 to 1 at 90 days<br>2.- Volume of hypoperfusion on brain CTP at 36h±24hours post MT<br>3.- Infarct Expansion Ratio (IER): Final infarct to initial ischemic tissue volumes on brain CTP at 36±24hours post MT.<br>4.- Barthel Scale score of 95 to 100, at 90 days.<br>5.- EuroQol Group 5-Dimension Self-Report Questionnaire (EQ-5D-3L) at 90 days<br>6.- Shift analysis of the modified Rankin Scale (mRS), at day 90 |
| **SAFETY OUTCOMES** | 1.- Mortality at 90 days.<br>2.- Symptomatic intracerebral hemorrhage (sICH ) rate at 24 hours. |
| **STUDY STATUS** | Recruitment |

# CHOICE-II Trial

**STUDY STATUS** Recruitment

**STUDY COMPLETION (Estimated)** May 2025




**Enrollment: 168/440**

CHOICE II

# Title: Predicting functional recovery in patients with intracerebral hemorrhage: multicenter validation of a new prognostic scale

(PRO-ICH score: **PRO**gnosis for **I**ntra**C**erebral **H**emorrhage )

**Coordinator Centers:**

Hospital Germans Trias i Pujol. Co-PI: Mònica Millán

Hospital de Sant Pau i de la Santa Creu. Co-PI: Anna Ramos

**Participating Centers:**

1. **Hospital Germans Trias I Pujol**
2. Hospital Dr. Josep Trueta
3. Hospital Clínico Universitario de Santiago de Compostela
4. Hospital Universitario Torrecárdenas
5. Hospital Universitario de Donosti
6. Hospital Moisès Broggi
7. Hospital Clínico Universitario de Valladolid
8. Hospital Universitario Central de Asturias
9. Hospital Universitario de A Coruña

# Previous results: Design and external validation

**Design Cohort**

Prospective
Unicentric (HGTiP)
March 2020 – April 2022

Sample size:
242 patients

**External validation Cohort**

Multicentric population registry
March 2020 – February 2022

Sample size:
334 patients

| Escala 5 | |
|---|---|
| NIHSS | |
| ≥20 | 5 |
| 5 – 20 | 2 |
| <5 | 0 |
| Volumen HIC | |
| ≥35ml | 1 |
| <35ml | 0 |
| Edad | |
| ≥75 años | 3 |
| 55 – 74 años | 2 |
| <55 años | 0 |
| Tiempo inicio - urgencias | |
| <6h | 1 |
| ≥6h | 0 |
| **Total** | **0-10** |

**-Better than the oICH scale**

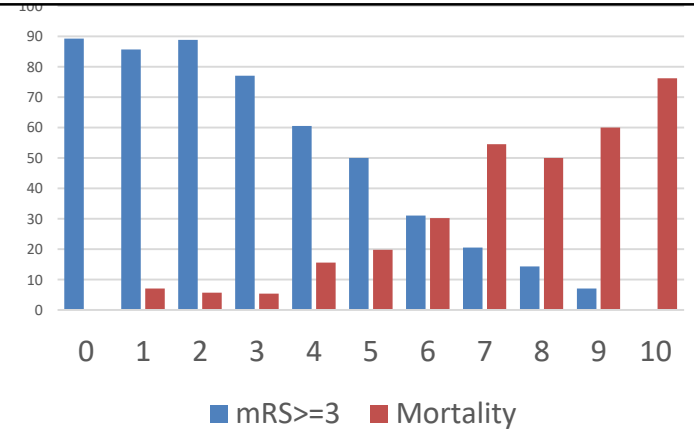
**-Generalizable**

**-Fewer and easier variables and categorizations**

**-Positive and negative clinical prognosis information**

**-Contemporary**

**-Designed and validated in patients treated to the maximum**



# Objectives

**PRIMARY OBJECTIVE**

- **To validate the predictive value of PRO-ICH** in determining **functional recovery at 90 days** in patients who have suffered intracerebral hemorrhage treated to the maximum **in real clinical practice.**

**SECONDARY OBJECTIVES**

- To validate in real clinical practice, the predictive value of PRO-ICH in determining **functional recovery , mortality and quality of life** assessed in the **long term** (6 months and 1 year) in patients who have suffered intracerebral hemorrhage treated to the maximum
- To compare the prognostic performance of the new score with the existing prognostic scores (oICH, mICH, ICH-GS, FUNG, Max-ICH) at 90 days
- To explore the association between baseline serum concentrations of **biomarkers** related to **iron metabolism, brain edema and neurofilament formation** and functional outcome at 90 days in patients who have suffered intracerebral hemorrhage treated to the maximum that could potentially **improve the predictive value of the PRO-ICH.**

# Study population (n= 1688 patients, 10 centers)


+ No AMT≤ 24 horas

mRS ≤ 3


3 m 6 m 12 m

mRS centralized blinded assessment

**Pro-ICH Score**

**Treatment "guidelines"**

**AES 2024**: Favorable, No financiable
**Pending allegations**

↓ *If definitive NOT*

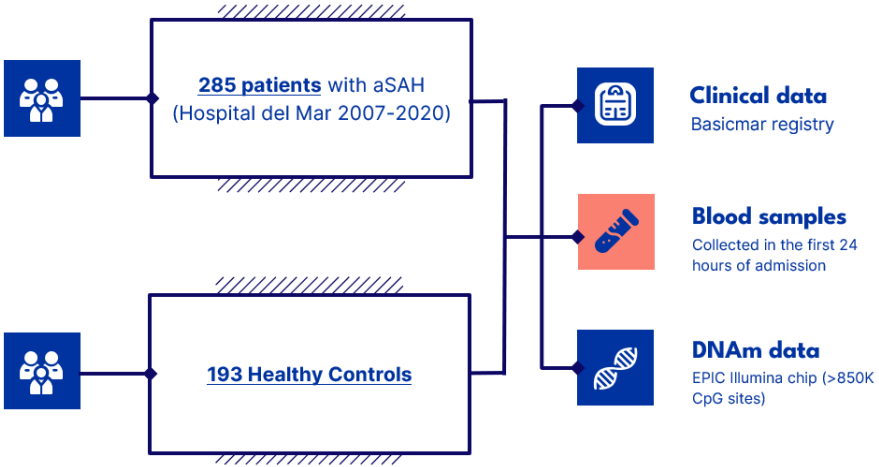
Local mRS assessment
Not biomarkers ?

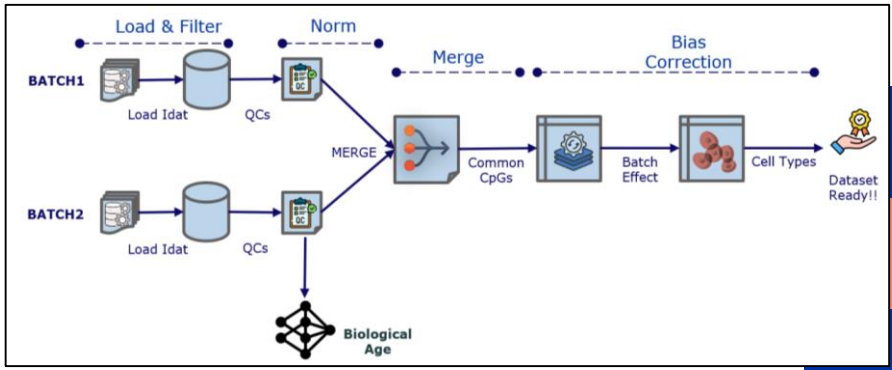
# EPICA study: EPIgenetic Changes in brain Aneurysms

**Promotor:** Instituto Hospital del Mar de Investigación biomédica

**Main Objective:** **To compare the DNA methylation (DNAm) signature between aneurysmal subarachnoid hemorrhage (aSAH) patients and control subjects.**

**Inclusion criteria:** Diagnosis of aSAH and availability of DNAm data



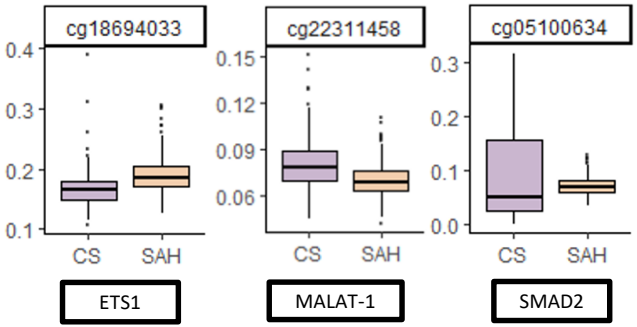

Hospital del Mar Research Institute
Barcelona

# EPICA study: EPIgenetic Changes in brain Aneurysms

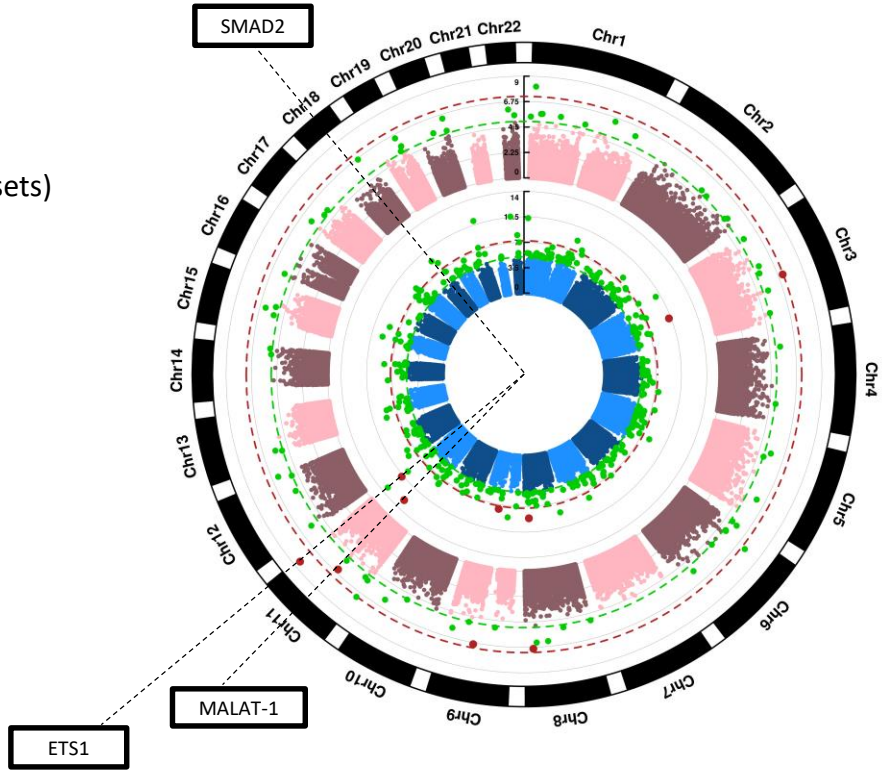
**Full Dataset** (Inner circle)
- 40 significant CpGs by Bonferroni

**Matched Dataset** (Outer circle)
- 19 significant CpGs by FDR

**Overlap** (Significant in Full & Matched Datasets)
- 5 significant CpGs
- Including ETS1 and MALAT-1




**Circular Manhattan Plot (Full + Matched)**




Hospital del Mar Research Institute
Barcelona

# EPICA study: EPIgenetic Changes in brain Aneurysms

**A distinctive DNAm signature can be found in patients experiencing aSAH in comparison with controls**

**- 5 significant CpGs** can be found associated with aSAH in both full and matched datasets.
- Two significant CpGs were annotated to **ETS1** and **MALAT-1**, both genes associated in previous studies with aneurysm risk / formation / progression.
- We found a significant CpG annotated to **SMAD2** in the full dataset, also associated with aneurysm formation.
- **36 significant DMRs** were found in an overlapped dataset, including ETS1 (2 CpGs) and MALAT-1 (5 CpGs)

**FUTURE STEPS**

- Perform pathway analyses
- Analyses stratified by sex
- Replicate the results including a larger cohort of cases and controls

# **GENVADER STUDY: GEN**ome-wide association study of **VA**sospasm and **DE**layed cerebral ischemia in aneurysmal suba**R**achnoid haemorrhage

**Promotor:** Instituto Hospital del Mar de Investigación biomédica

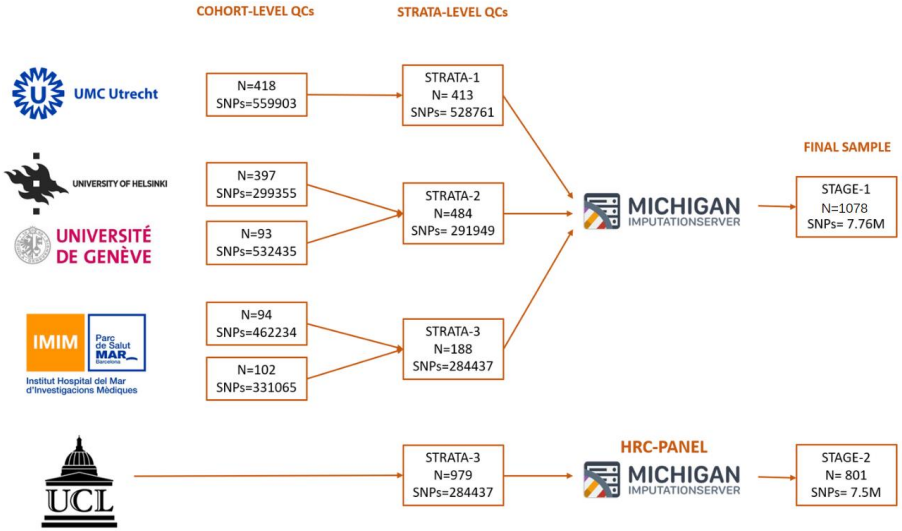
**Main Objective: Identify genetic variants associated with vasospasm and DCI**

Type of collaboration: Multicenter study with clinical and genetic data.

Inclusion criteria :

- Patients over 18 years old diagnosed with aSAH

-GWAS data or blood samples

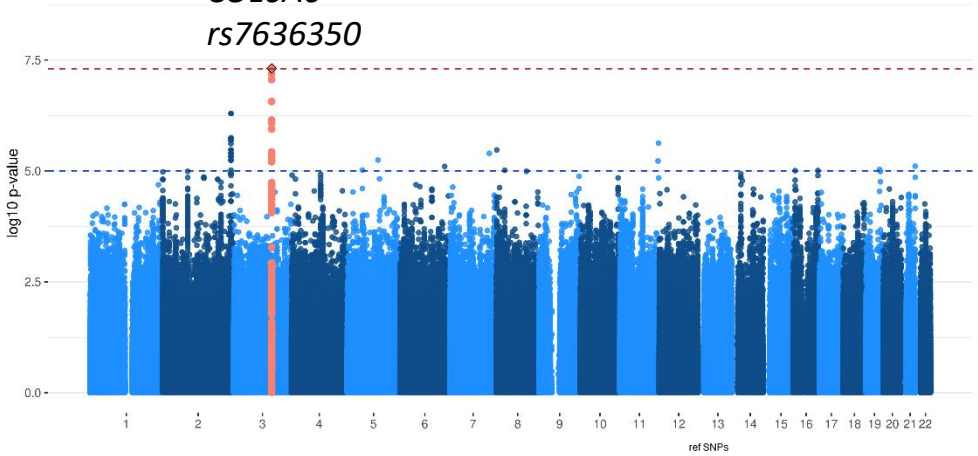


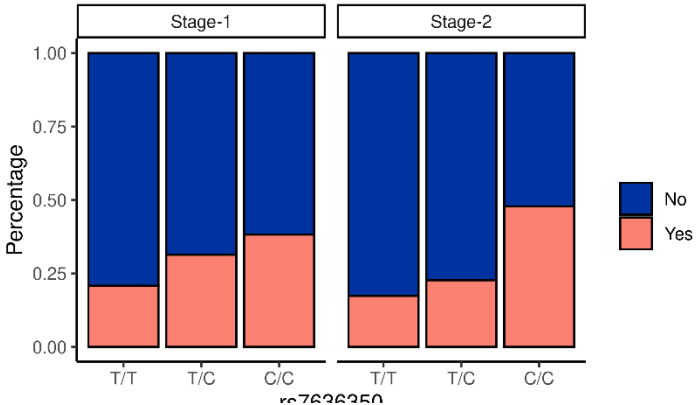

Hospital del Mar Research Institute Barcelona

# GENVADER STUDY: GENome-wide association study of VAsospasm and DElayed cerebral ischemia in aneurysmal subaRachnoid haemorrhage

**Current status:** GWAS and PostGWAs analysis completed. Writing a manuscript

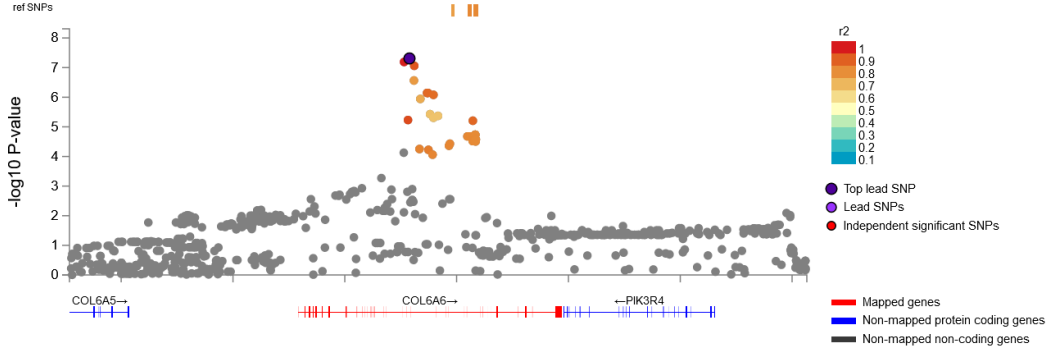
*COL6A6*
*rs7636350*




**COL6A6 Collagen Type 6 Alpha 6 Chain:**

Nervous system development
Assembly of collagen fibrils
Signal Transduction
Collagen biosynthesis and modifying enzymes
Degradation of the extracellular matrix




Hospital del Mar Research Institute Barcelona

# GENVADER STUDY: GENome-wide association study of VAsospasm and DElayed cerebral ischemia in aneurysmal subaRachnoid haemorrhage

**Future steps:**

-**Replicate the results in the future with a larger cohort including other Spanish groups from RICORs** (Hospital Clínic and Hospital de Sant Pau from Barcelona)

-Perform a Multi-trait analisis (MTAG) with DCI and outcome including summary statistics of other GWAS (Gaastra et al. ) from other groups within the International Stroke genetics consortium

-To create a poligenic risk score for DCI and outcome using different methods (Plink LDpred, Lassosum)

-Stratifiy the results by sex

# **EPICAS study: EPI**genetic **C**hanges in **A**neurismal **S**ubaracnoid hemorrhage

**Promotor:** Instituto Hospital del Mar de Investigación biomédica.

**Main Objective:** **To identify epigenetic variants associated with the development of complications and prognosis after aneurysmal subarachnoid hemorrhage aSAH.**

**Type of collaboration:** Multicenter study with clinical and genetic data

**Inclusion criteria**:
- Patients over 18 years old diagnosed with aSAH
- Individual epigenetic data (EWAS) and/or DNA or whole blood sample extracted during the acute phase of the hemorrhage

Hospital del Mar Research Institute Barcelona

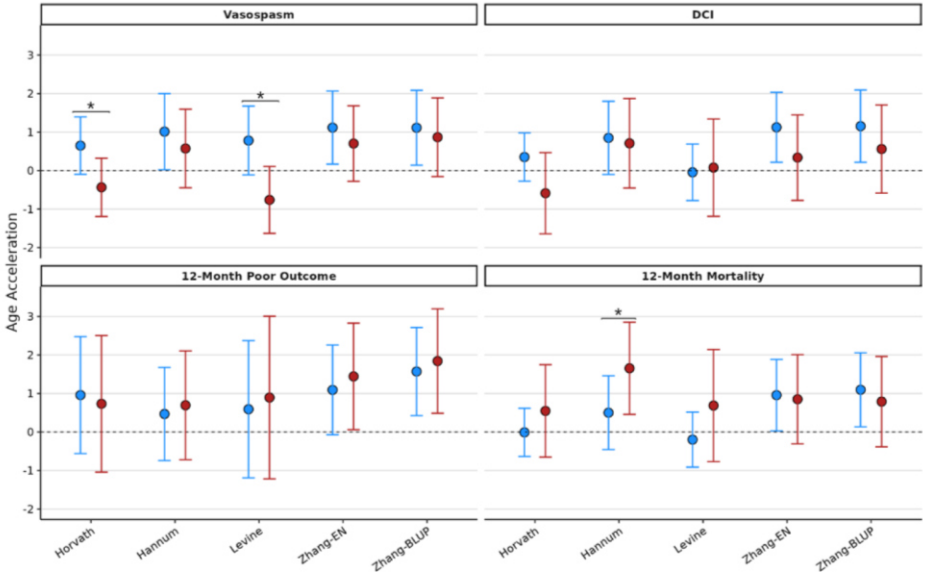
# **EPICAS study:** **EPI**genetic **C**hanges in **A**neurismal **S**ubaracnoid hemorrhage

***The influence of epigenetic biological age on key complications and outcomes in aneurysmal subarachnoid haemorrhage***.

Macias A. et al. J Neurol Neurosurg Psychiatry 2024 (in press).

288 samples from hospital del Mar analyzed with EWAS.

**Epigenetic biological age has been associated with Delayed Cerebral Ischemia (DCI) and outcome.**



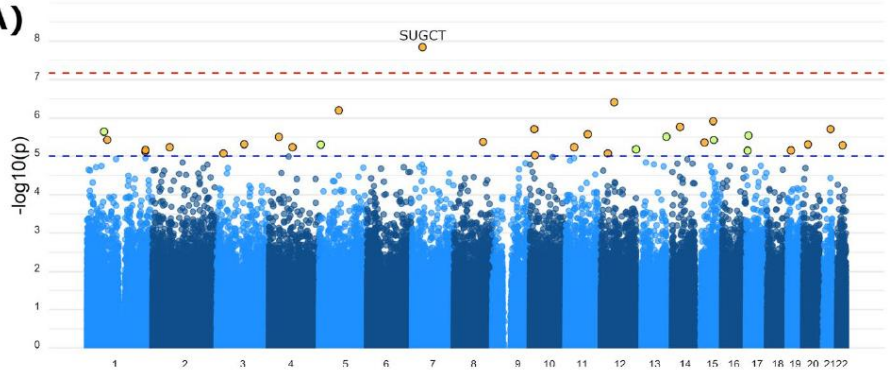

Hospital del Mar Research Institute
Barcelona

# **EPICAS study: EPI**genetic **C**hanges in **A**neurismal **S**ubaracnoid hemorrhage

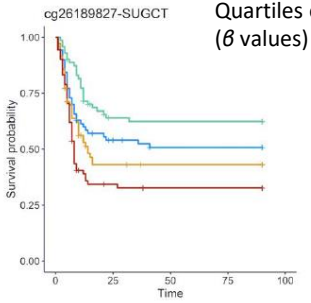
***Blood DNA Methylation Analysis Reveals a Distinctive Epigenetic Signature of Vasospasm in Aneurysmal Subarachnoid Hemorrhage***. Fernández-Pérez I et al. Transl Stroke Res 2024 (in press).

EWAS analysis comparing cases with and without vasospasm in aSAH revealed that **cg26189827 annotated to SUCGT gene is associated with vasospasm.**

A)




B)




Quartiles of methylation (*β* values)

**Future steps:**

-Replicate in new cases (Hospital Mar and Hospital Clinic de Barcelona)
-Mediation analyses
-Stratify by Sex
-Influence of Chromosome X

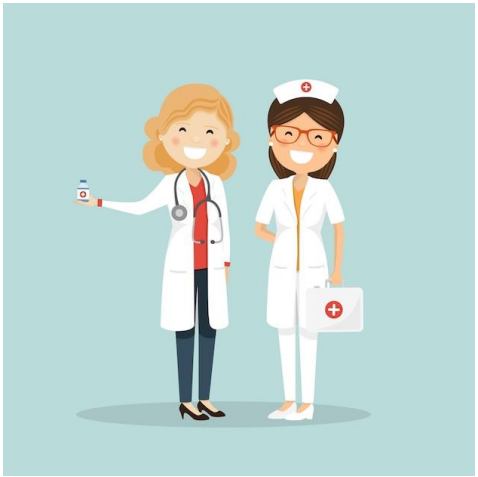
Hospital del Mar Research Institute Barcelona

**INGLES_MC**

# Validation of a screening protocol for groin complications in stroke patients undergoing endovascular procedures (**INGLES_MC**)

**DONOSTIA UNIVERSITY HOSPITAL/BIOGIPUZKOA IS** IP: Patricia de la Riva and Arantza Lopez de Turiso

1. **Hospital Universitario Donostia**
2. **Hospital Universitario Basurto**
3. **Hospital Universitario de Cruces**
4. **Hospital Universitario de Araba**
5. **Hospital Clinic de Barcelona**
6. **Hospital Germans Trias i Pujol**
7. **Hospital Universitario Torrecárdenas**
8. **Hospital Universitario de la Fé**
9. **Hospital Universitario Ramón y Cajal**
10. **Hospital Universitario Fundación Jiménez Díaz**



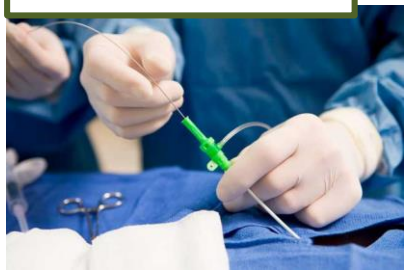
20 investigadores formados (18 enfermeras/os)

# Aims and methods

To determine whether a **screening protocol for groin complications using ultrasonography** is implementable and feasible in stroke units

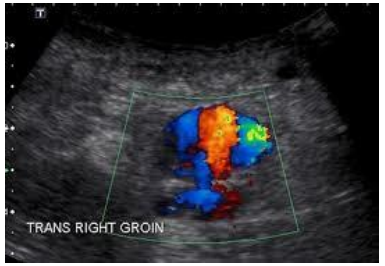
To describe the incidence of local complications associated with endovascular procedures through the use of this protocol in a multicenter study

10 Stroke Units



PROTOCOL

Physical examination
- Pulses
- Hematoma
- Lump
- Pain
- Auscultation



# Current status: ongoing (recruiting)

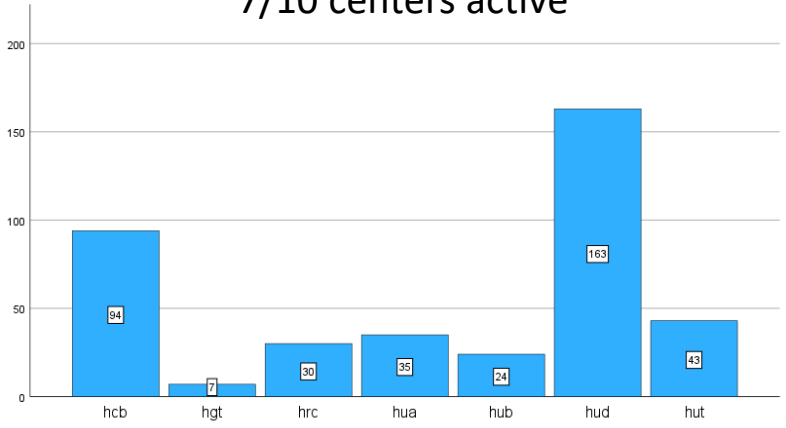
December 2023: Training course

January 2024: Recruitment start

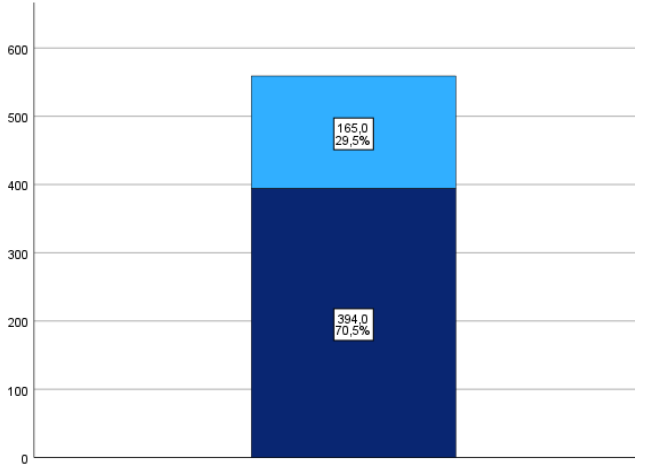
March 2025: End of the study (objective 1000 patients)

June 2025: Results

7/10 centers active




Inclusion: 70.5% of patients treated with EVT (394/559 patients)



Germans Trias i Pujol Hospital

IGTP Institut de Recerca Germans Trias i Pujol

# Evaluating Lung Injury as a TargEt against Stroke-Associated Pneumonia (ELITE-SAP)


**PROMOTER**

Hospital Universitari Germans Trias i Pujol, IGTP

Alejandro Bustamante

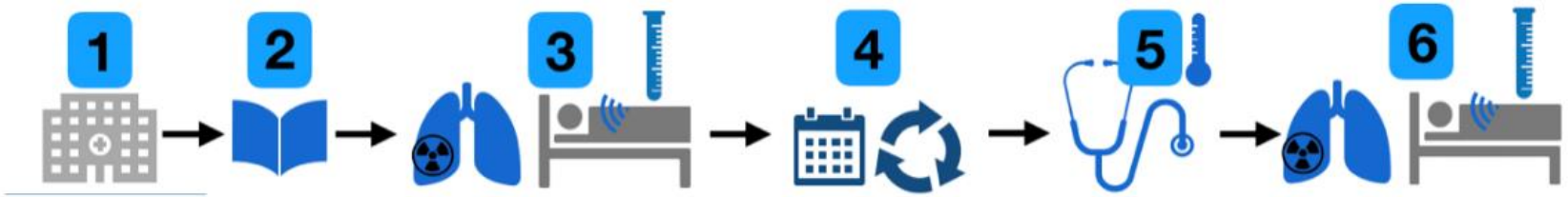
Marina Martínez Sánchez


**PARTICIPANTS**

1. Hospital Germans Trias i Pujol
2. Hospital Universitario 12 de Octubre
3. Hospital Moisès Broggi
4. Hospital Universitario de Valladolid

## OBJECTIVES

- To validate a **biomarker panel** to predict SAP in patients with severe stroke
- To validate a biomarker panel to rule-out SAP in stroke patients with infectious symptoms/signs
- To evaluate **lung ultrasound** as a tool for SAP prediction or diagnosis




**STROKE UNIT ADMISSION**
Inclusion / exclusion criteria
Informed consent
REDCap inclusion

**BASELINE VISIT**
Baseline information
Chest X-Ray + lung US
Blood sample

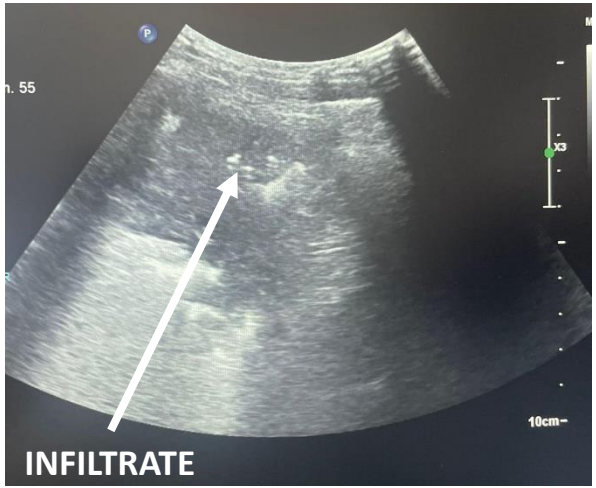
**DAILY FOLLOW-UP**
Days 1-7
mCDC criteria
NIHSS

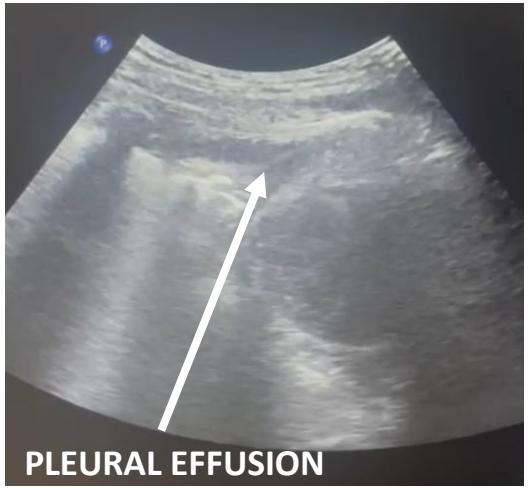
**SUSPECTED INFECTION**
Clinical workup: labs, CXR, cultures
Lung US
Blood sample

**3 MONTHS**
mRS

# STUDY PROGRESS

- Enrollment will finish in Dec-2025
- Pre-established simple size 150 (estimated rate of infections 1/3)
- Currently N=50 but infection rate close to 50%
- Biomarker measurements at the end of the project
- Lung ultrasound images: feasible and reproducible between examiners
- **NEW SITES WELCOME!**



RICORS-ICTUS | Instituto de Salud Carlos III