

# ACST-2 MRI substudy

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## An update

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**ACST-2 Collaborators' Meeting  
Valencia, 24<sup>th</sup> - 25<sup>th</sup> September 2018**

# Background:

## New DWI lesions after carotid interventions

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- ICSS-MRI substudy 2010

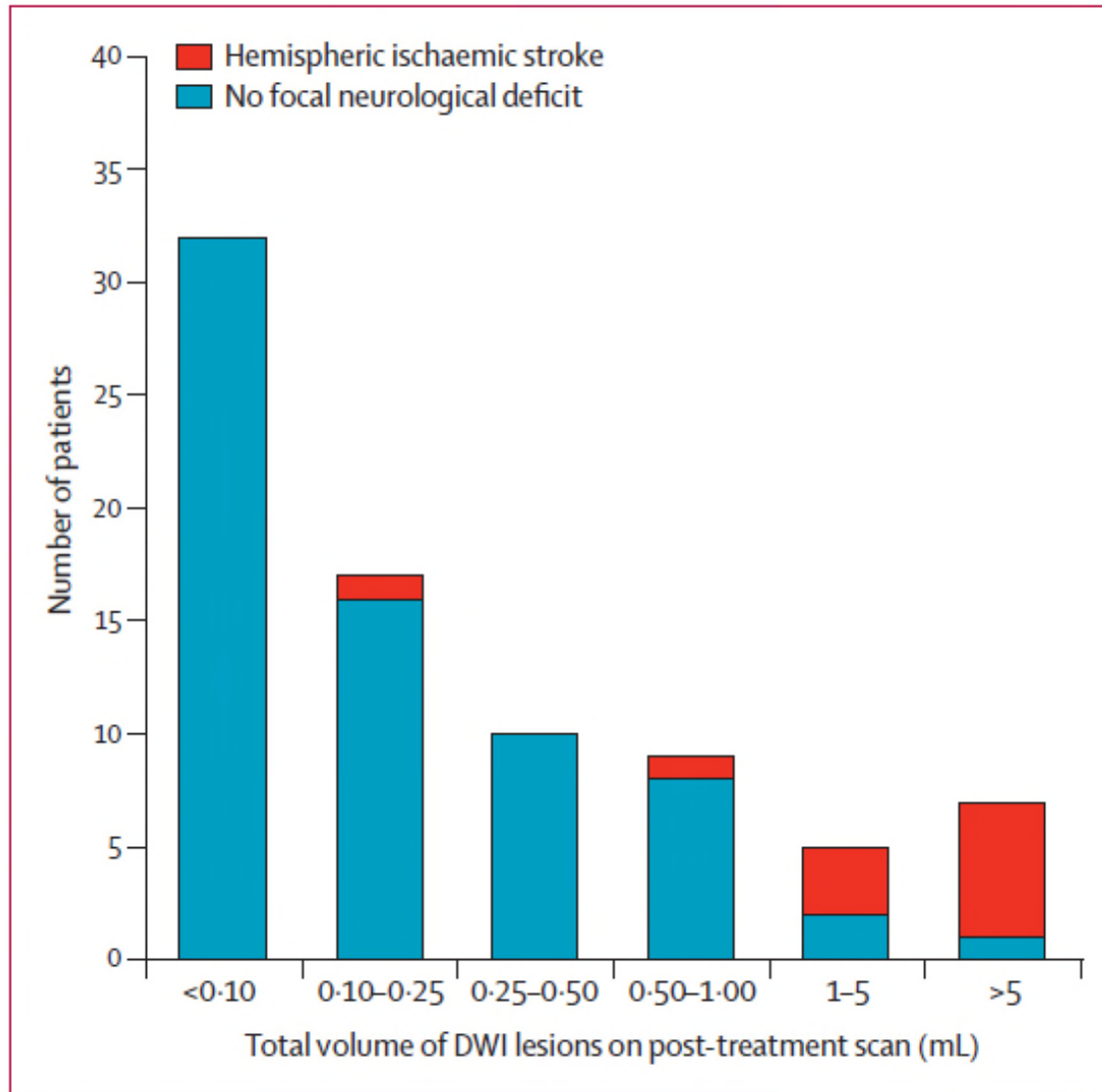
	<b>CAS</b> (n=124)	<b>CEA</b> (n=107)	Adjusted OR (95% CI), p
<b>≥1 new DWI lesion</b> <i>N patients (%)</i>	<b>62</b> <b>(50%)</b>	<b>18</b> <b>(17%)</b>	5.21 (2.78-9.79), p<0.001

- Kuliha et al. 2015

	Carotid endarterectomy (n = 73)	Carotid angioplasty and stenting (n = 77)	P†
Ipsilateral new brain infarctions	18 (25)	38 (49)	0.002
Volume of ischaemic lesion (cm <sup>3</sup> )*	0 (0–0.025)	0 (0–0.250)	0.010‡
New brain infarctions > 0.5 cm <sup>3</sup>	9 (12)	10 (13)	1.000
New brain infarctions in both hemispheres	0 (0)	15 (19)	< 0.001

# Background

## ICSS-MRI substudy



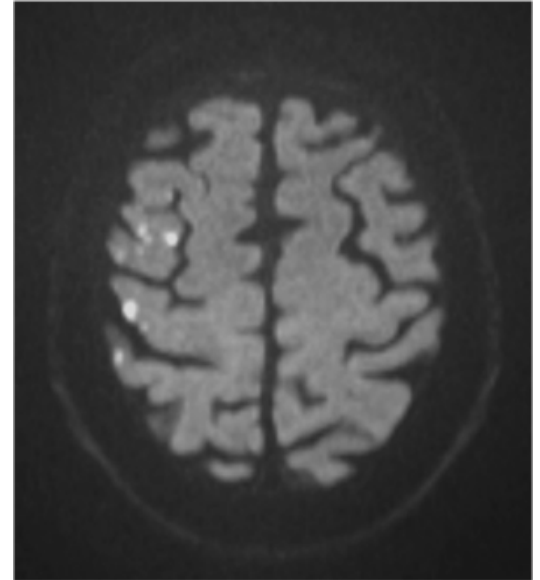
Higher total lesions volumes in patients with stroke than in those with silent lesions ( $p < 0.001$ )

# Background:

## Brain MRI in carotid interventions

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- MRI is sensitive in detecting cerebral embolism
  - Most MRI lesions are asymptomatic
  - MRI lesions correlate with stroke risk
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- → MRI is a useful **surrogate outcome measure** to investigate treatment effects and potential modifiers thereof within clinical trials
  - MRI can be analysed blinded to treatment



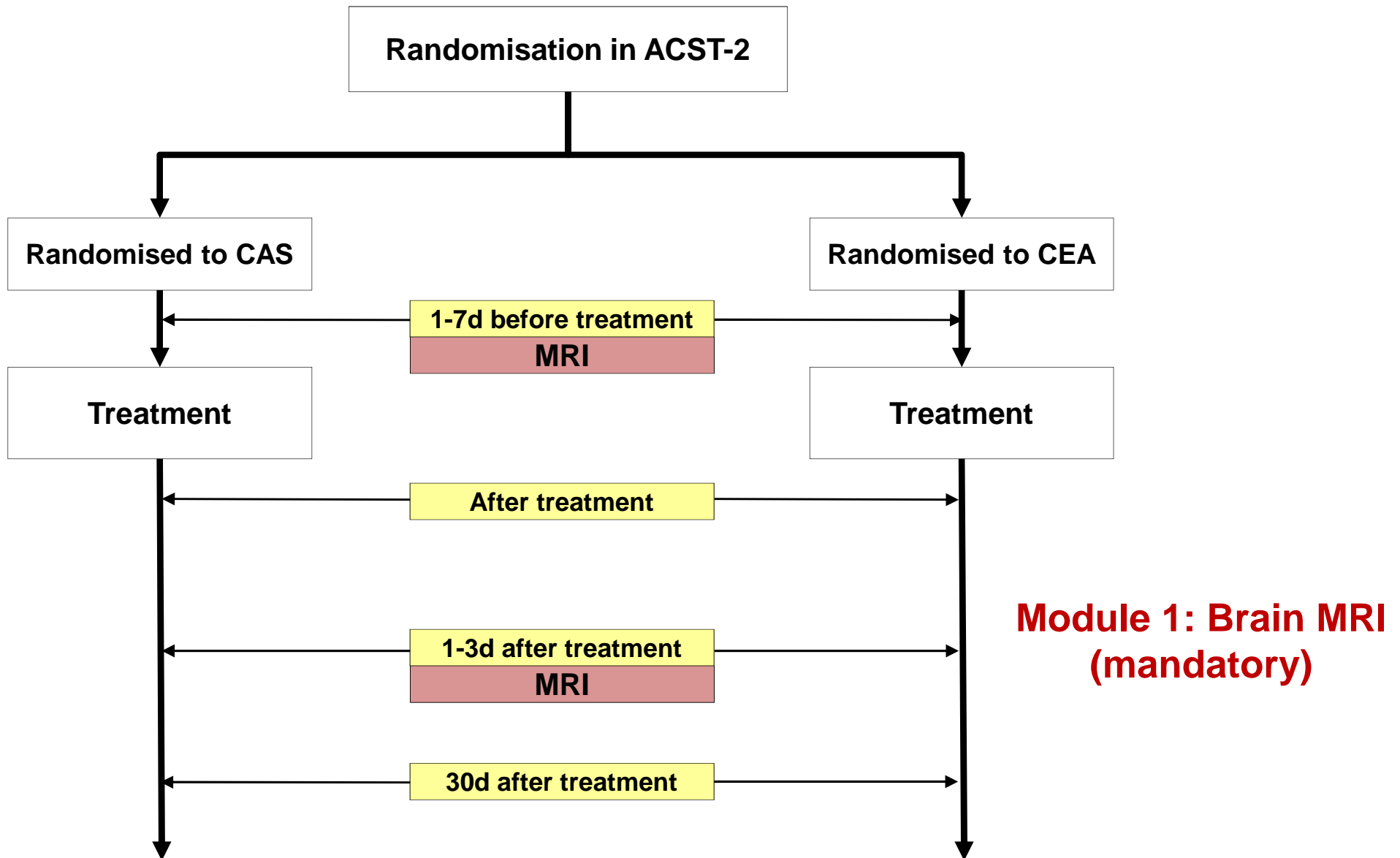
# ACST-2 MRI substudy

## Objectives

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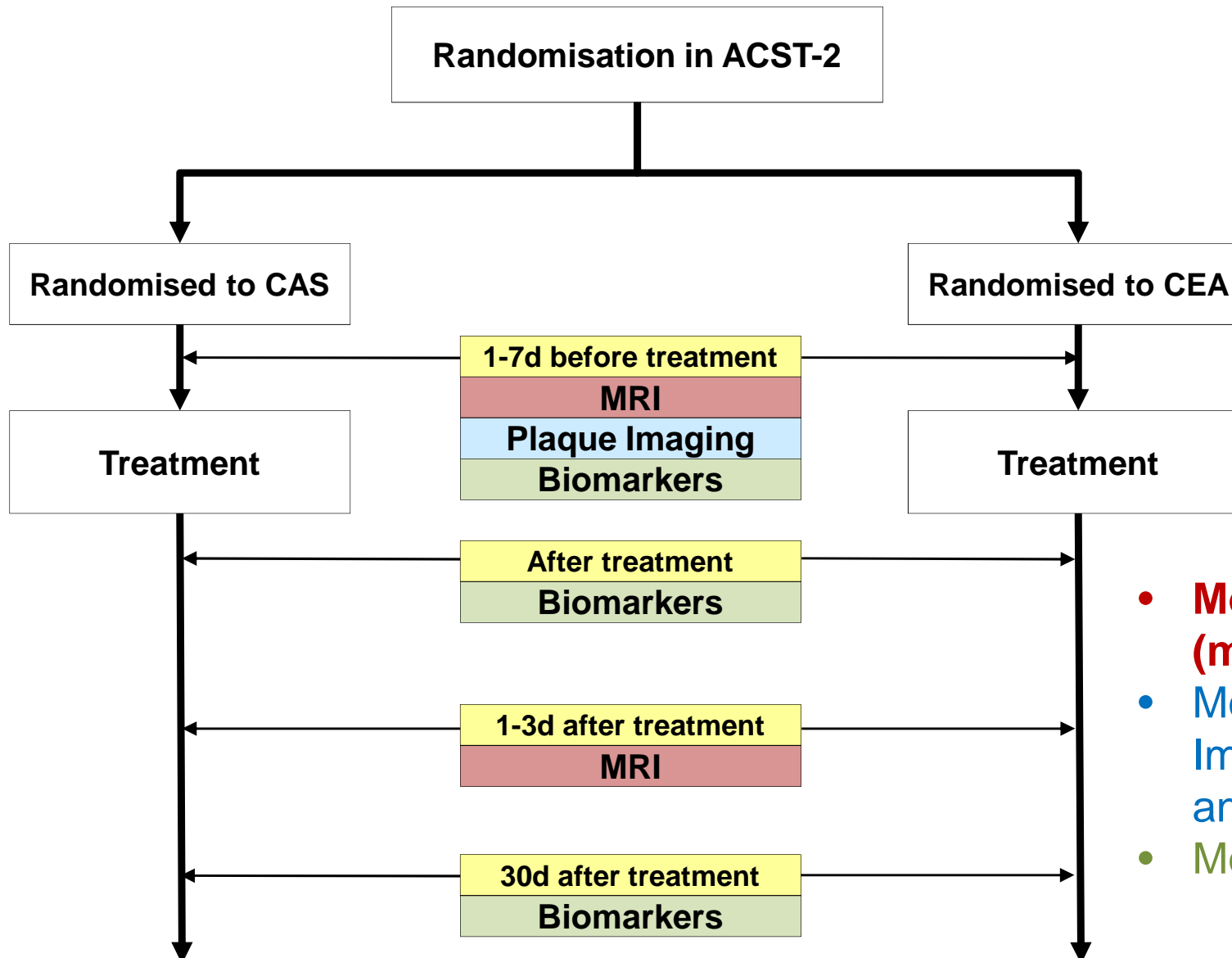
- To compare the incidence of symptomatic and silent cerebral ischaemia between CAS and CEA using MRI as blinded, surrogate outcome assessment
- To investigate whether plaque imaging and vascular anatomy predict cerebral ischaemia in CAS or CEA

# ACST-2 MRI substudy: Study flow chart



**CAS:** carotid artery stenting, **CEA:** carotid endarterectomy

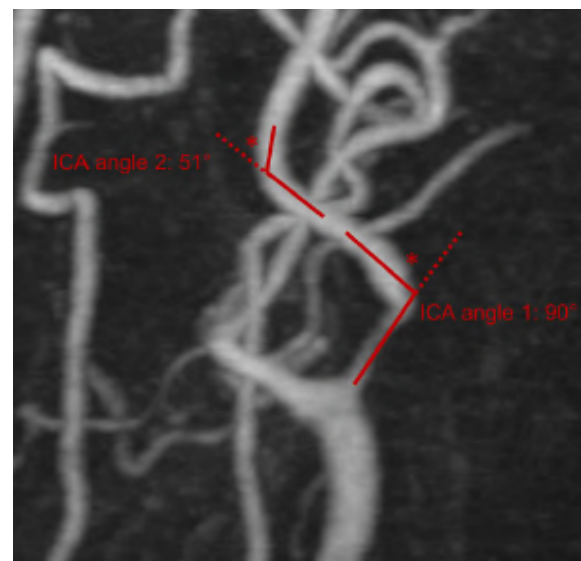
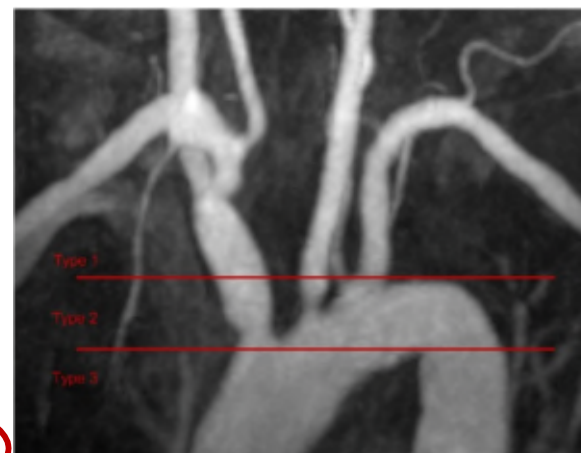
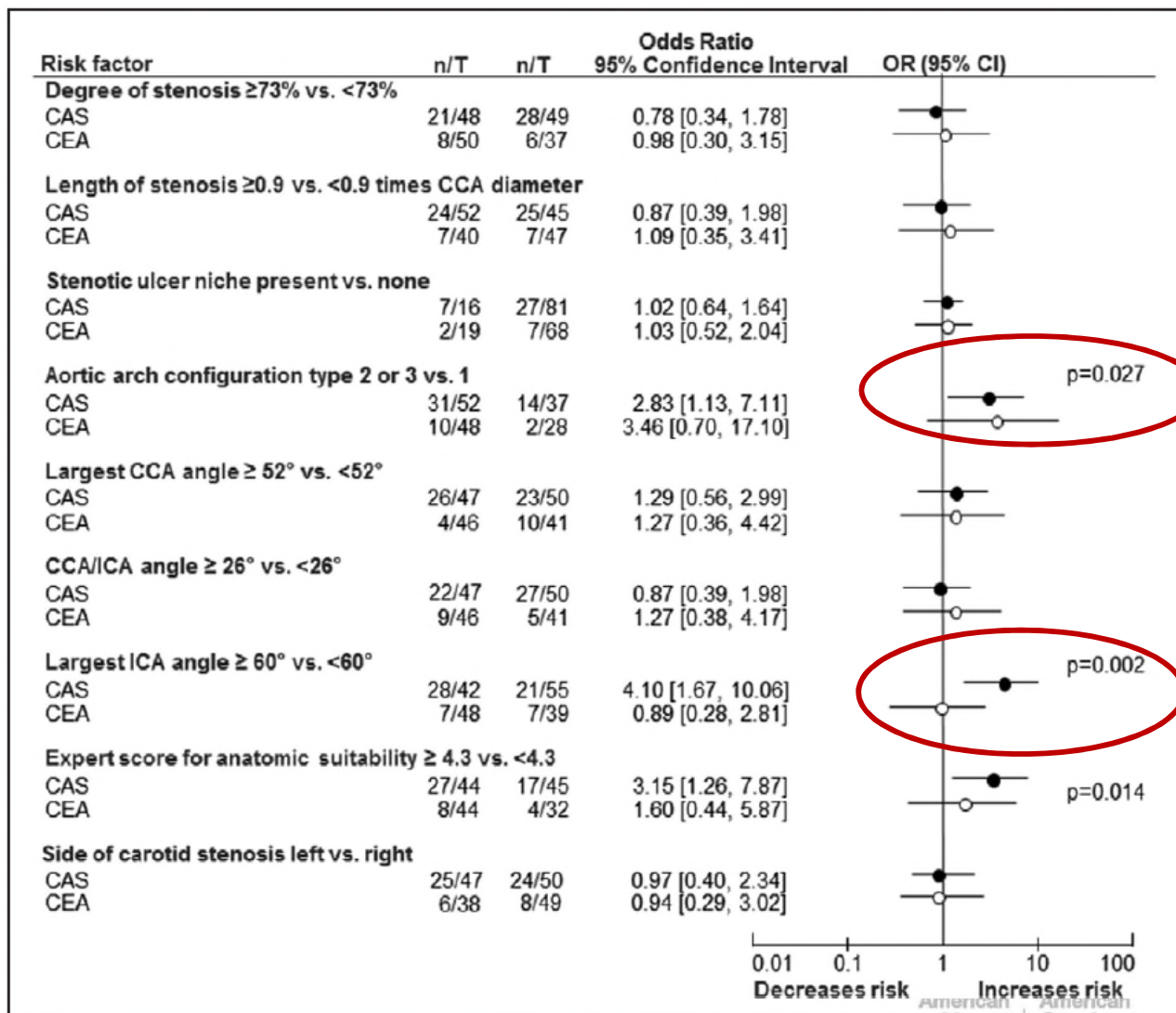
# ACST-2 MRI substudy: Study flow chart



- **Module 1: Brain MRI (mandatory)**
- **Module 2: Plaque Imaging (Ultrasound and/or MRI)**
- **Module 3: Biomarkers**

**CAS:** carotid artery stenting, **CEA:** carotid endarterectomy

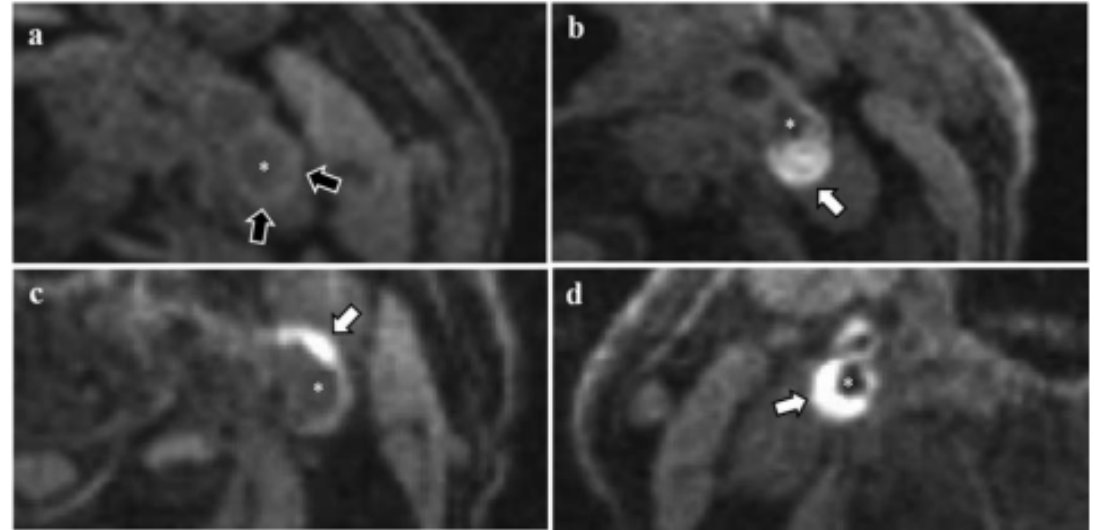
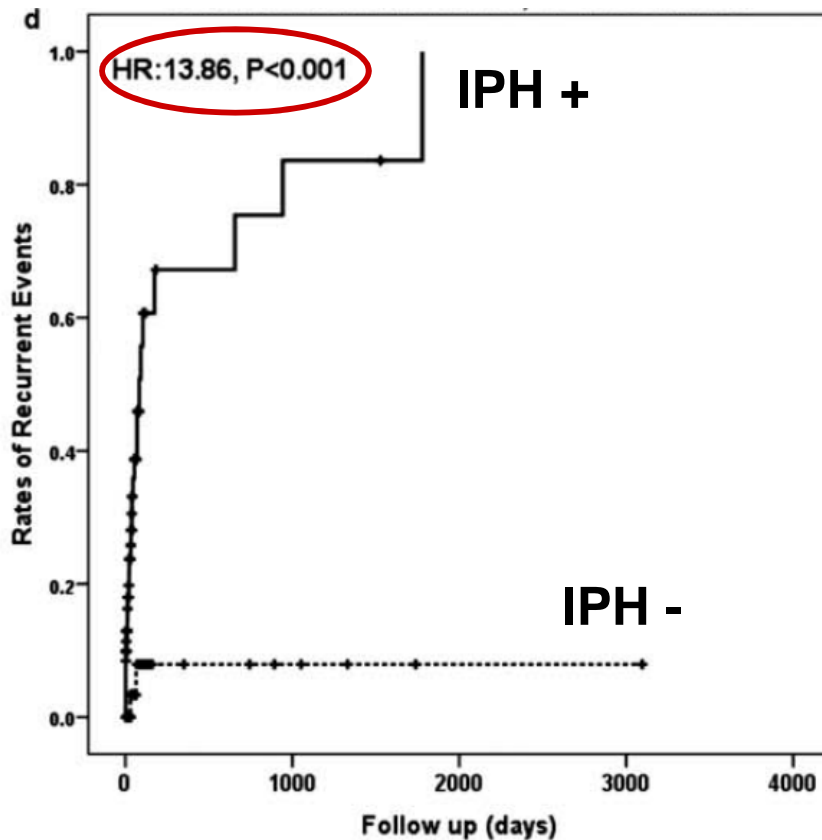
# Vascular anatomy predicts risk of CAS





# MRI Plaque Imaging Intra-plaque haemorrhage

Recurrent ischaemic events  
70-99% carotid stenosis



- 179 patients with symptomatic carotid stenosis  $\geq 50\%$
- Follow-up of up to 9 years

# MRI Plaque Imaging

## Intra-plaque haemorrhage





























	Participants (N)	Hazard Ratio (95% CI)	P-Value
<b>Age</b>			
< 65 yrs*	105	1.00	
65-74 yrs	150	0.88 (0.37 - 2.07)	0.76
> 74 yrs	303	0.74 (0.33 - 1.66)	0.46
<b>Sex</b>			
Male*	384		
Female	174	1.05 (0.52 - 2.13)	0.89
<b>Diabetes mellitus</b>			
no*	125		
yes	189	1.73 (0.95 - 3.17)	0.07
<b>Hypertension</b>			
no*	189		
yes	369	1.09 (0.55 - 2.18)	0.8
<b>Degree of stenosis</b>			
< 50%*	186	1.00	
50 - 69%	191	2.00 (0.96 - 4.20)	0.066
70 - 99%	181	3.37 (1.46 - 7.79)	0.004
<b>Type of qualifying event</b>			
Stroke*	284	1.00	
TIA	200	1.1 (0.62 - 1.95)	0.75
Retinal ischaemia (incl. Retinal infarction and AmF)	74	0.36 (0.10 - 1.23)	0.10
<b>IPH at inclusion</b>			
no*	271		
yes	287	10.81 (4.72 - 24.76)	< 0.001

# Participating centres & enrolment

Patient numbers per treatment (ACST-2, pre- and post-treatment MRI) (6 lines)			
Centre	Total	CAS	CEA
1 Istituto Auxologico Italiano IRCCS	4	4	0
2 Sapienza University of Rome	5	4	0
3 University Hospital Basel	46	25	21
4 University Hospital of Larissa	22	12	10
5 University Medical Center Utrecht	16	10	6
6 Total	93	55	37

- Centres which have not entered their data do not appear
- Please enrol **both** CAS and CEA patients in the substudy

# Participating centres & enrolment

Patient	Eligibility	Visit 0	Treatment	Visit 1	Visit 2	Visit 3	Study Termination	Adverse Events
BIOPLQ-BG033								
BIOPLQ-BG059								
BIOPLQ-BG071								
BIOPLQ-BG996								

- Please complete data entry for all your patients
- Only patients with complete data entry can be used for analysis
- Please let us know if you have questions or need new logins for the database

# Log for patients not included in substudy

**New patient**

Select a project: < Please choose >  
ACST-2 patients not included in MRI substudy (1.0.1)  
BIO-PLAQUE (1.5.6)

Patient was randomised to	<input type="radio"/> CAS <input checked="" type="radio"/> CEA
Any contraindication to MRI ...	<input checked="" type="radio"/> yes <input type="radio"/> no <input type="radio"/> unknown
... including	<input type="checkbox"/> Claustrophobia <input checked="" type="checkbox"/> Metal implant incompatible with MRI <input type="checkbox"/> Cardiac pacemaker incompatible with MRI <input type="checkbox"/> Other
Patient does not consent to MRI	<input type="radio"/> yes <input checked="" type="radio"/> no
MRI scanner unavailable <u>before</u> treatment	<input type="radio"/> yes <input type="radio"/> no <input checked="" type="radio"/> unknown
MRI scanner unavailable <u>after</u> treatment	<input type="radio"/> yes <input type="radio"/> no <input checked="" type="radio"/> unknown
Other reasons	<input type="radio"/> yes <input checked="" type="radio"/> no

Please complete data entry for all your ACST-2 patients **NOT included** in MRI substudy at your centre

# Participating centres & enrolment

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- **128 patients** are currently enrolled
- Active centres:
  - ❖ University Hospital Basel (CH): **46**
  - ❖ University Hospital of Larissa (GR): **30**
  - ❖ UMC Utrecht (NL): **17**
  - ❖ Serbian Clinical Centre Belgrade (RS): **11**
  - ❖ Istituto Auxologico Milano (IT): **11**
  - ❖ Klinikum rechts der Isar München (DE): **8**
  - ❖ La Sapienza Rome (IT): **5**
  - ❖ **NEW SITE:** Novosibirsk Research Institute of Circulation Pathology (RU)

# Centre remuneration & contact details

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**400 Euros** per patient with completed pre- and postprocedural MRI scan AND completed eCRF  
(Swiss Heart Foundation, grant extended until 12/2019)

Do you need further information or are interested in joining?

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**Thank you for your attention!**

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