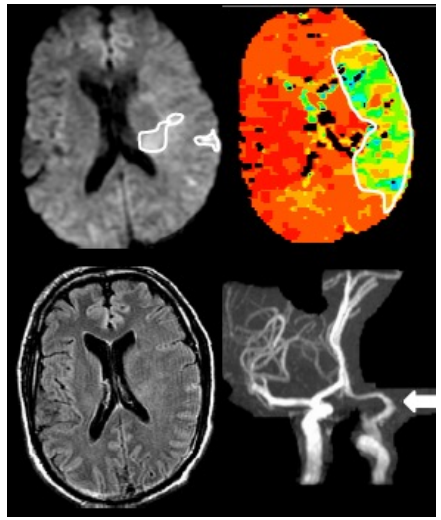

Quelles stratégies de reperfusion à la phase aiguë de l'infarctus cérébral ?

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Marseille

C2VN Centre de Recherche en CardioVasculaire et Nutrition

Centre de Recherche en CardioVasculaire et Nutrition
UMR AMU – INSERM – INRAE
Faculté des Sciences Médicales et ParaMédicales
Marseille

Aix*Marseille université
Initiative d'excellence

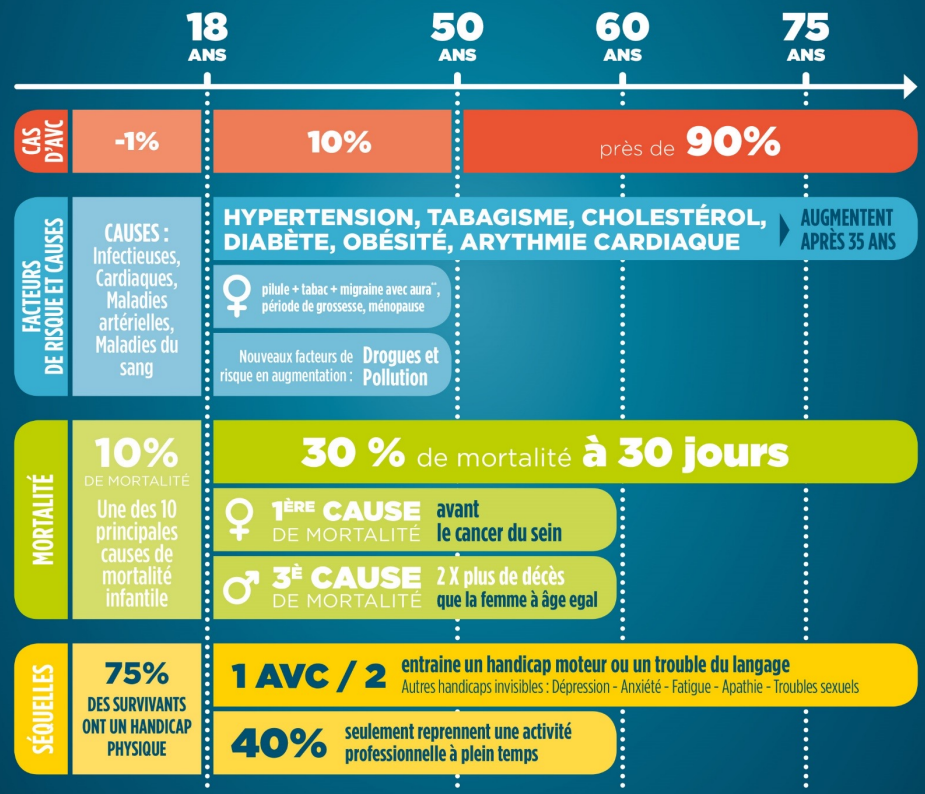
Faculté des sciences médicales et paramédicales
Aix*Marseille Université

SFNV
SOCIÉTÉ FRANÇAISE NEURO-VASCULAIRE

L'AVC NOUS SOMMES TOUS CONCERNÉS !

+ DE 140 000 VICTIMES D'AVC / an en France
DONT 32 000 AIT*

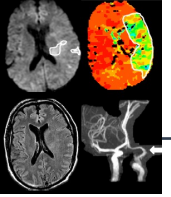
L'AVC est UNE DES PRINCIPALES CAUSES DE MORTALITÉ en France et dans le monde	1 PERSONNE SUR 6 AURA UN AVC dans sa vie	1/3 DES PATIENTS gardent un HANDICAP



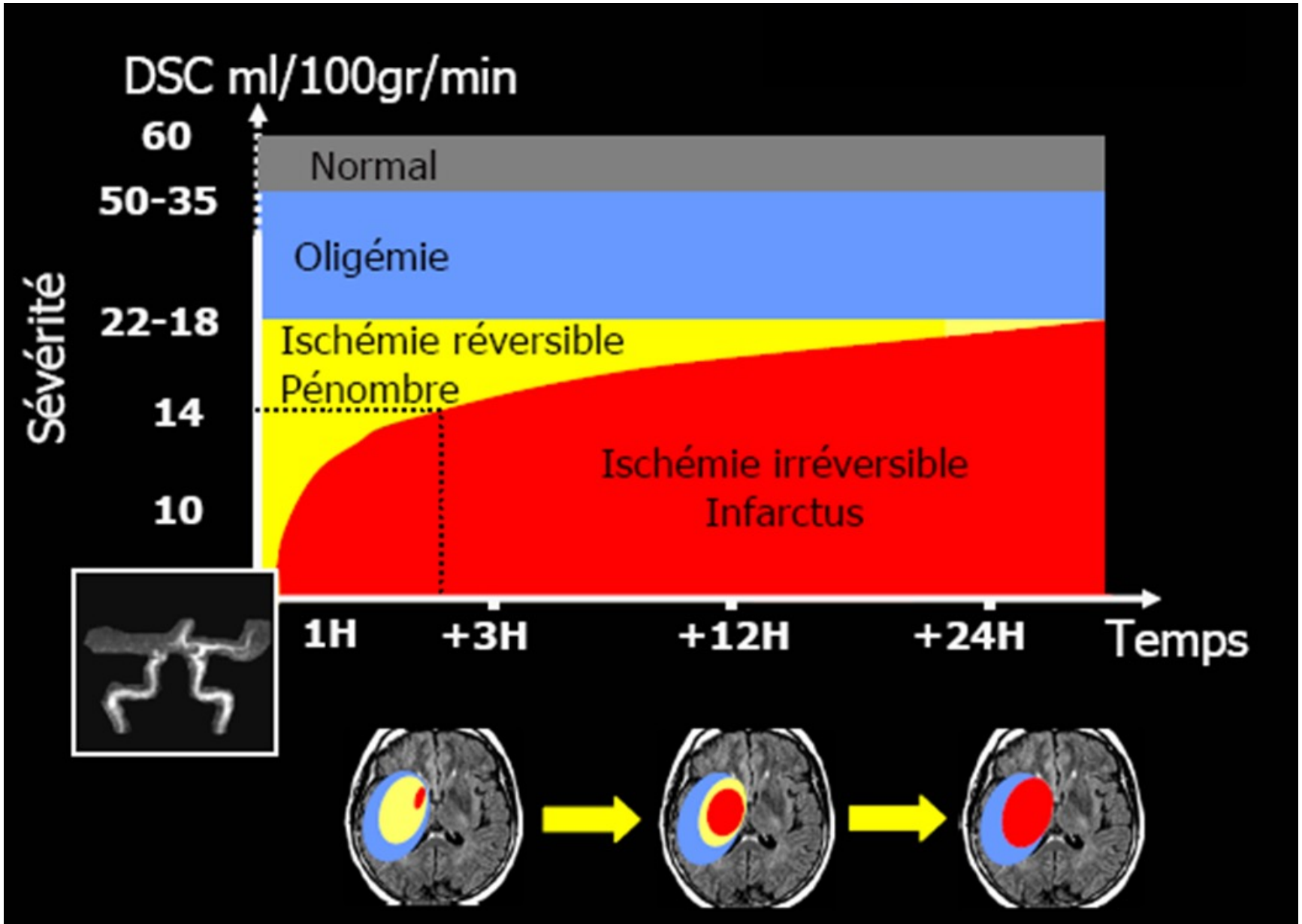
*AIT : Accident ischémique transitoire (alerte AVC)
**Migraines avec troubles visuels, sensitifs, aphasiques

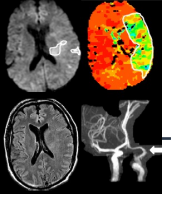
www.societe-francaise-neurovasculaire.fr / www.accidentvasculairecerebral.fr

Sources : "L'accident vasculaire cérébral en France : patients hospitalisés pour AVC en 2014 et évolutions 2008-2014" BEH 5 | 21 février 2017 ; pp 84-94. // "Mortalité par accident vasculaire cérébral en France en 2013 et évolutions 2008-2013" BEH 5 | 21 février 2017 ; pp 95-100.

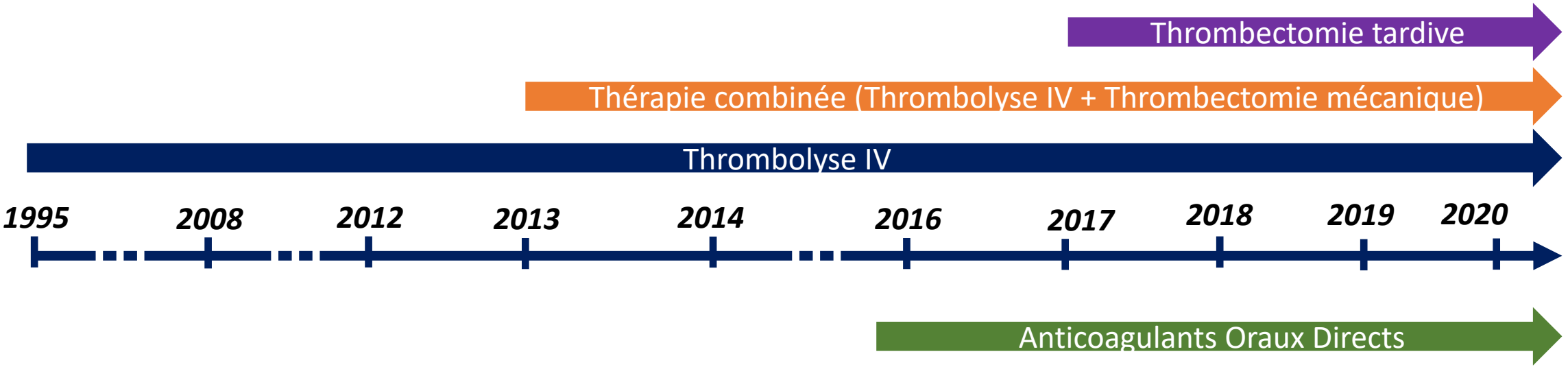


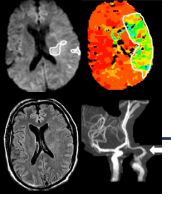
Recanaliser pour sauver la pénombre ischémique



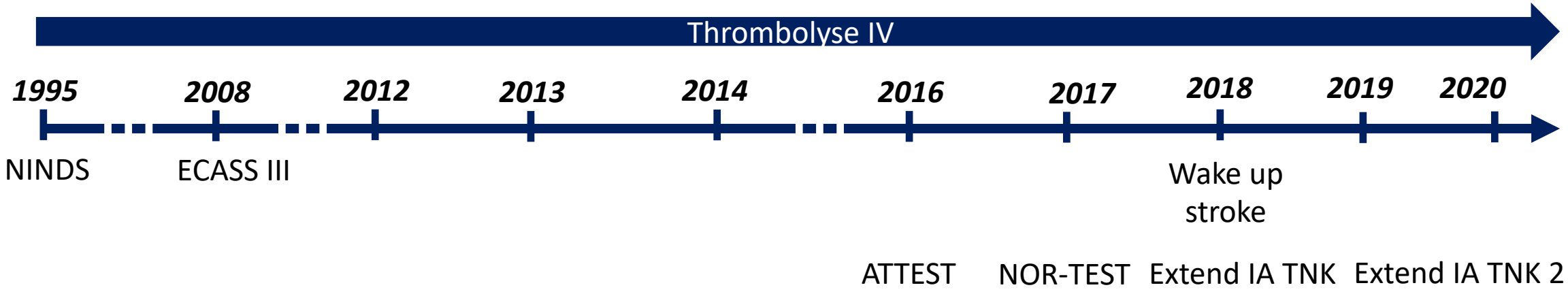


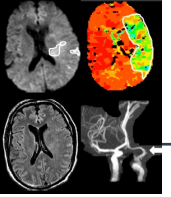
Evolution des traitements de recanalisation de l'infarctus cérébral





Thrombolyse IV



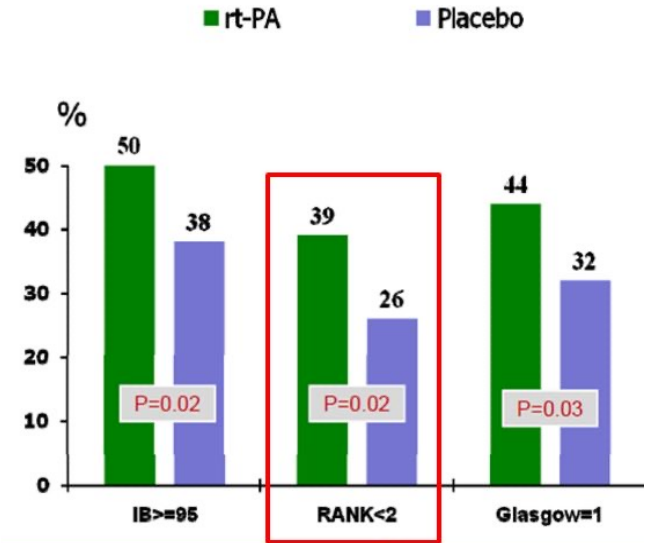


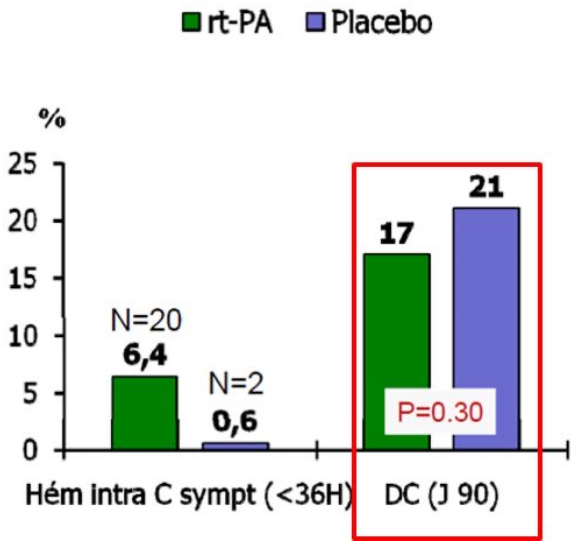
rt-PA IV : l'étude princeps

- **Etude NINDS (1995):**
  - Efficacité du rt-PA dans les 3ères heures: réduction du nombre de patients dépendants à 3 mois.
  - Tolérance du rt-PA: pas d'augmentation significative des décès.

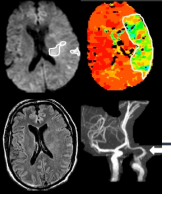
Score	Handicap
0	Aucun symptôme.
1	Pas de handicap significatif
2	Handicap léger
3	Handicap modéré
4	Handicap modérément sévère
5	Handicap sévère
6	Décès

Echelle de Rankin modifié (mRS)





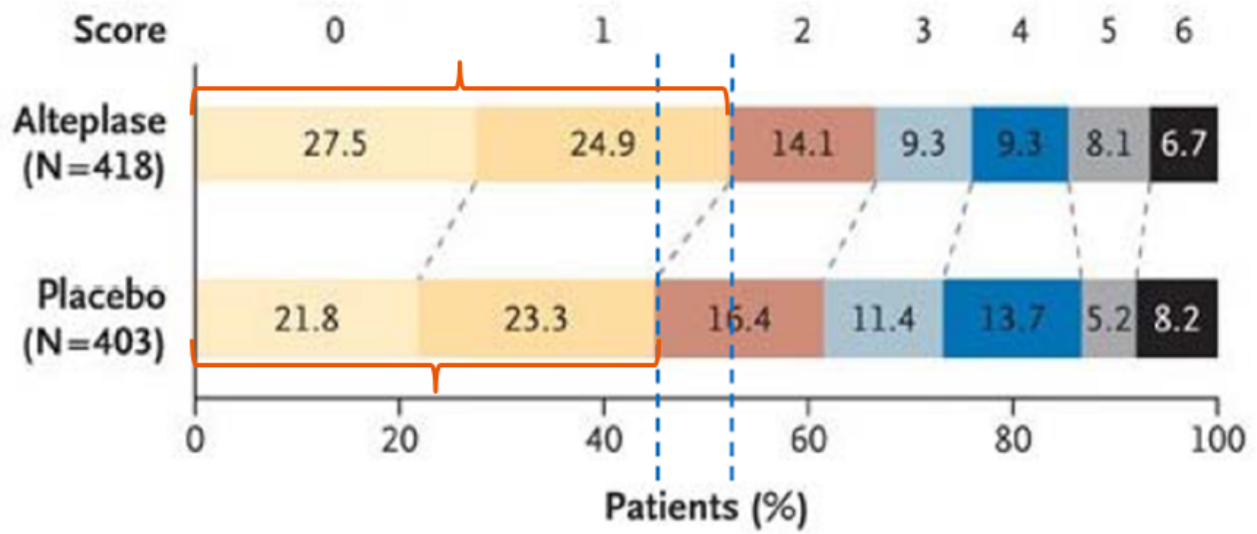
National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. **Tissue plasminogen activator for acute ischemic stroke**. *N Engl J Med.* 1995



rt-PA IV: évolution de la fenêtre thérapeutique

L'étude ECASS III (3-4,5H):

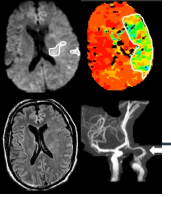
- 821 patients
- rt-PA IV (0,9 mg/kg) entre 3h et 4h30 (n=418) ou placebo (n=403)
- Rankin 0-1 à 90 jours



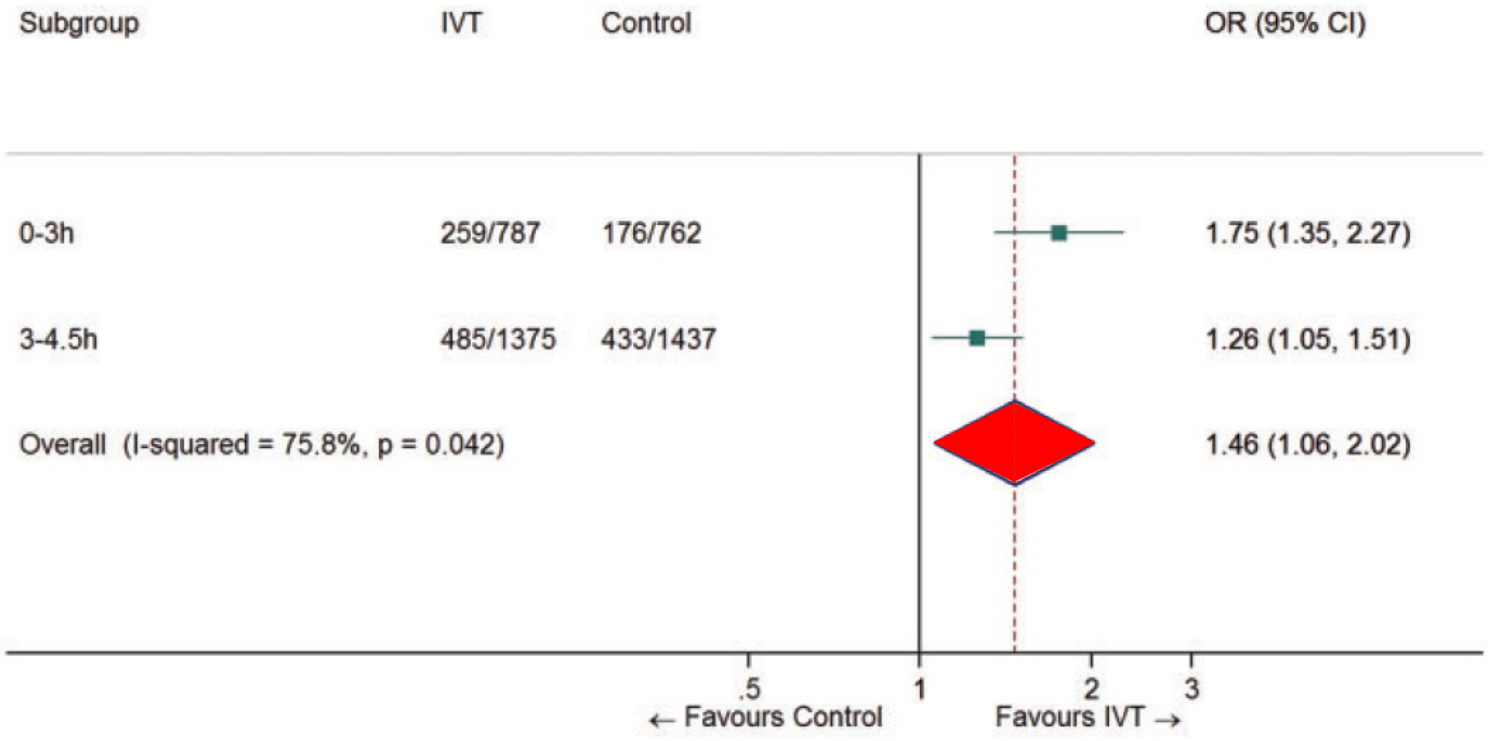
Δ + 7.2 %

Δ=7.2% (52.4% vs 45.2%)
RR=1.16 (1.01 – 1.34)

Hacke W, et al. ECASS Investigators. **Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke.** *N Engl J Med*. 2008



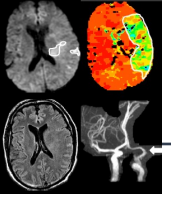
L'efficacité démontrée du rt-PA IV jusqu'à 4h30



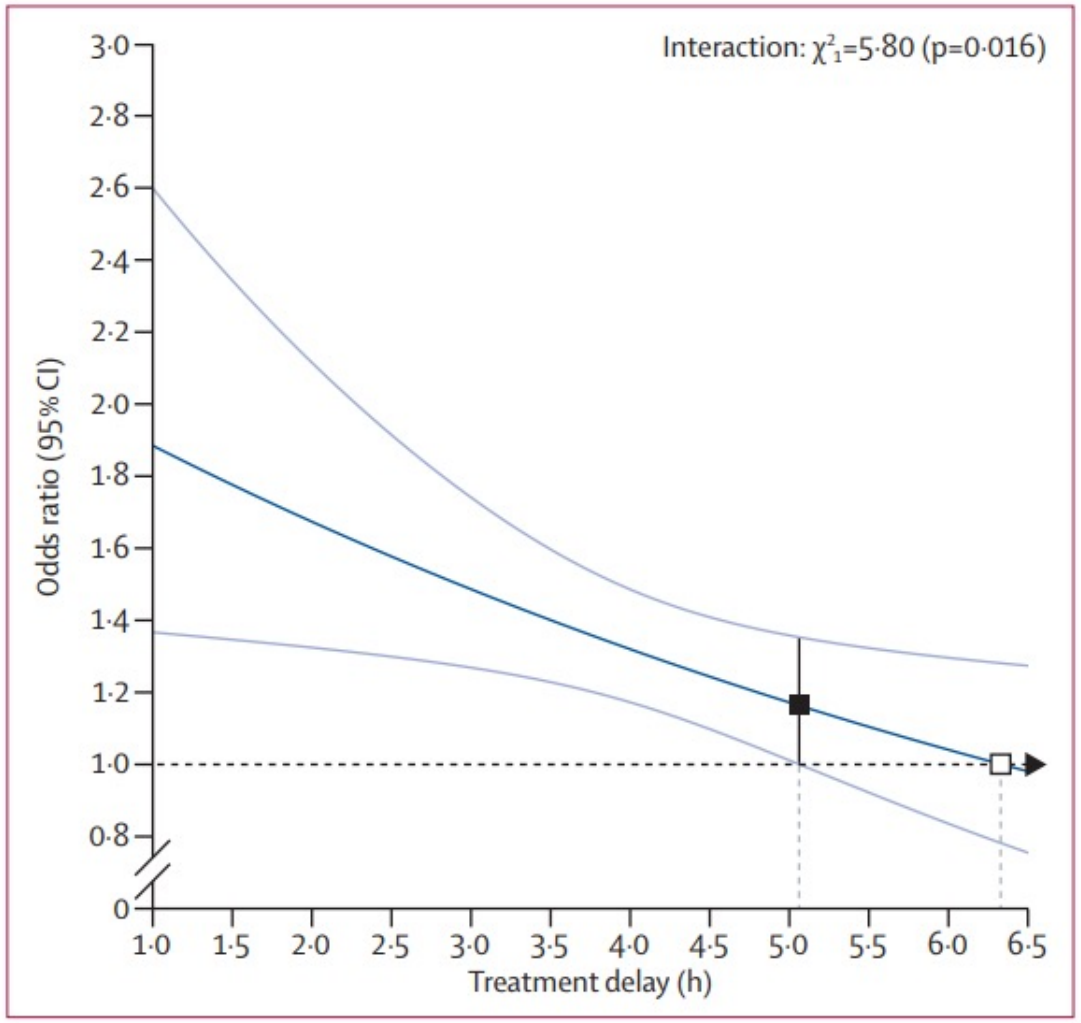
American Heart Association | American Stroke Association
life is why

1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over ~~1 minute~~) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known ~~well or at baseline~~ state. Physicians should review the criteria outlined in Table 6 to determine patient eligibility.	I
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 ~~minute~~) ~~is also recommended~~ for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient ~~last known well~~. Physicians should review the criteria outlined in Table 6 determine patient eligibility.	I

Emberson J *et al.* **Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials.** *Lancet 2014*.

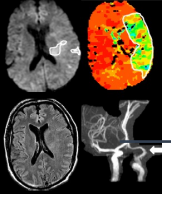


« Time is Brain »

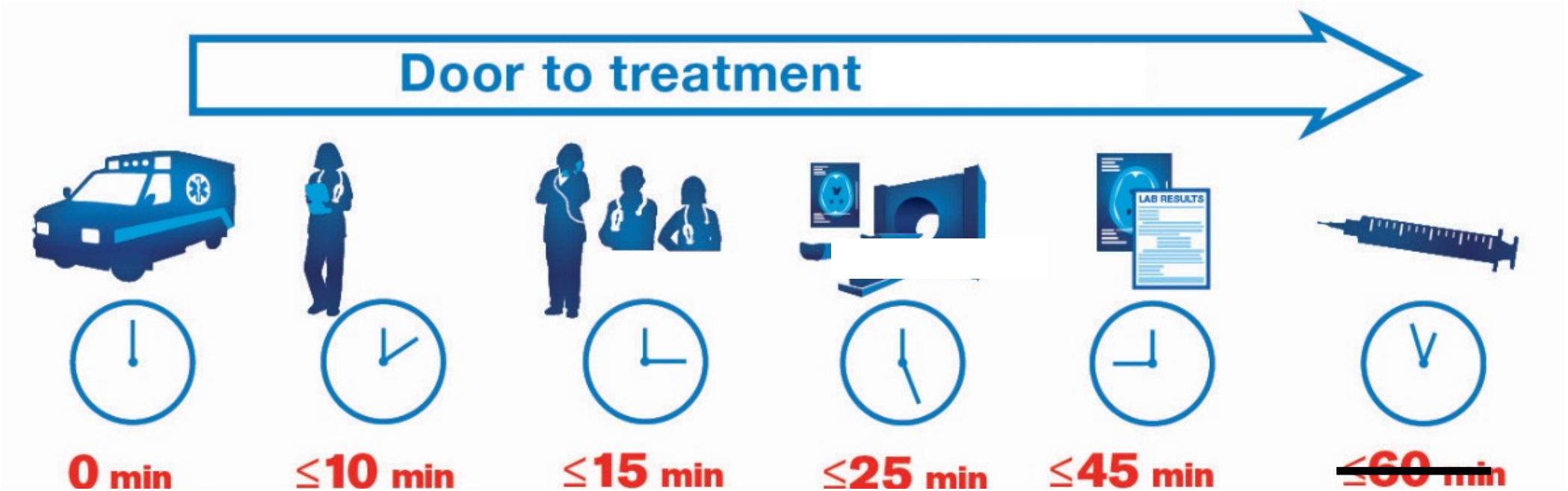


Stroke : Time lost is brain lost

Emberson J *et al.* **Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials.** *Lancet 2014*.



« Time is Brain »

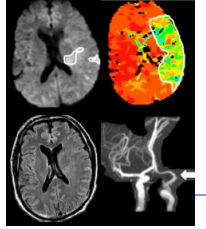


≤ 45 min

American Heart Association | American Stroke Association
life is why

In patients eligible for IV alteplase, benefit of therapy is time dependent, and treatment should be initiated as quickly as possible.

I



Fibrinolyse cérébrale:
En pratique

Indications (SFNV):

Déficit neurologique brutal et focal révélant un infarctus cérébral,

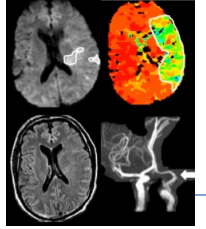
Heure de début des signes <4H30,

Possibilité d'injecter le rt-PA dans les 4H30,

Imagerie validée (IRM ou TDM).

HAS
HAUTE AUTORITÉ DE SANTÉ

La thrombolyse IV peut être envisagée après 80 ans jusqu'à 3 heures (accord professionnel).



Fibrinolyse cérébrale:
Quelle imagerie initiale

RECOMMANDATIONS DE BONNE PRATIQUE

HAS

Accident vasculaire cérébral : prise en charge précoce (alerte, phase préhospitalière, phase hospitalière initiale, indications de la thrombolyse)

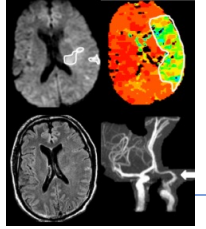
Mai 2009

Les patients suspects d'AVC aigu doivent avoir un accès prioritaire 24 h/24 et 7 j/7 à l'imagerie cérébrale. Des protocoles de prise en charge des patients suspects d'AVC aigu doivent être formalisés et contractualisés entre le service accueillant ces patients et le service de radiologie (accord professionnel).

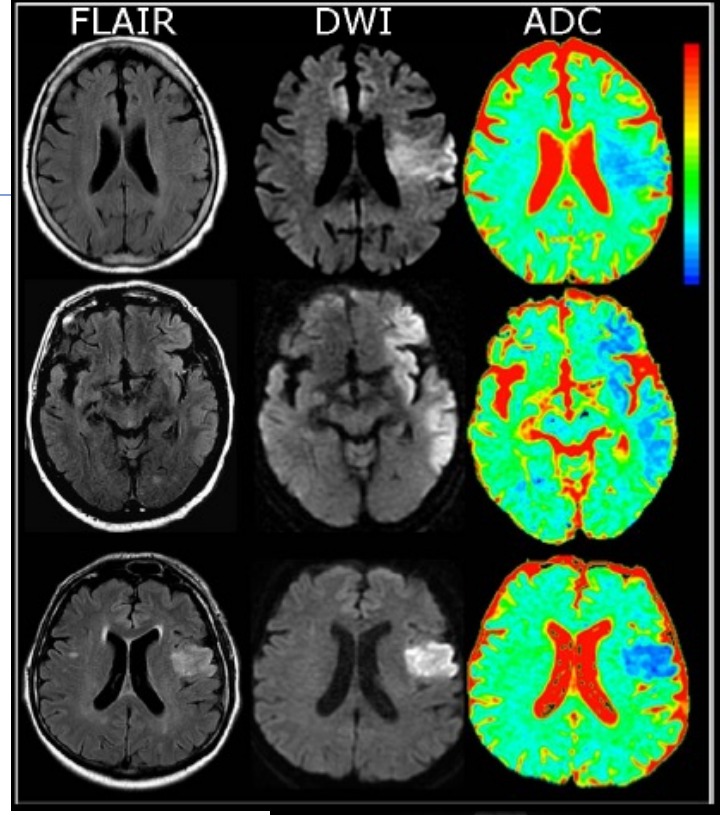
L'IRM est l'examen le plus performant pour montrer précocement des signes d'ischémie recente, et elle visualise l'hemorragie intracrânienne. Il convient de la réaliser de façon privilégiée.

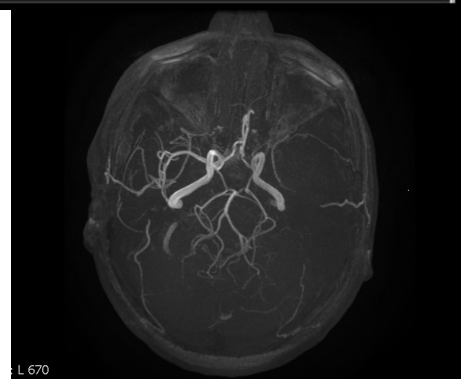
Si l'IRM est possible comme examen de première intention, elle doit être accessible en urgence et elle doit privilégier des protocoles courts incluant les séquences suivantes : diffusion, FLAIR, écho de gradient (grade B).

En cas d'impossibilité d'accéder en urgence à l'IRM, il convient de réaliser un scanner cérébral. Cet examen ne montre qu'inconstamment des signes d'ischémie récente, mais permet de visualiser une hémorragie intracrânienne.



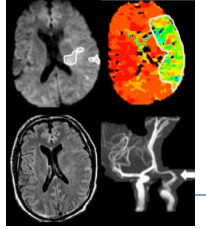
Fibrinolyse cérébrale:
Quelle imagerie initiale





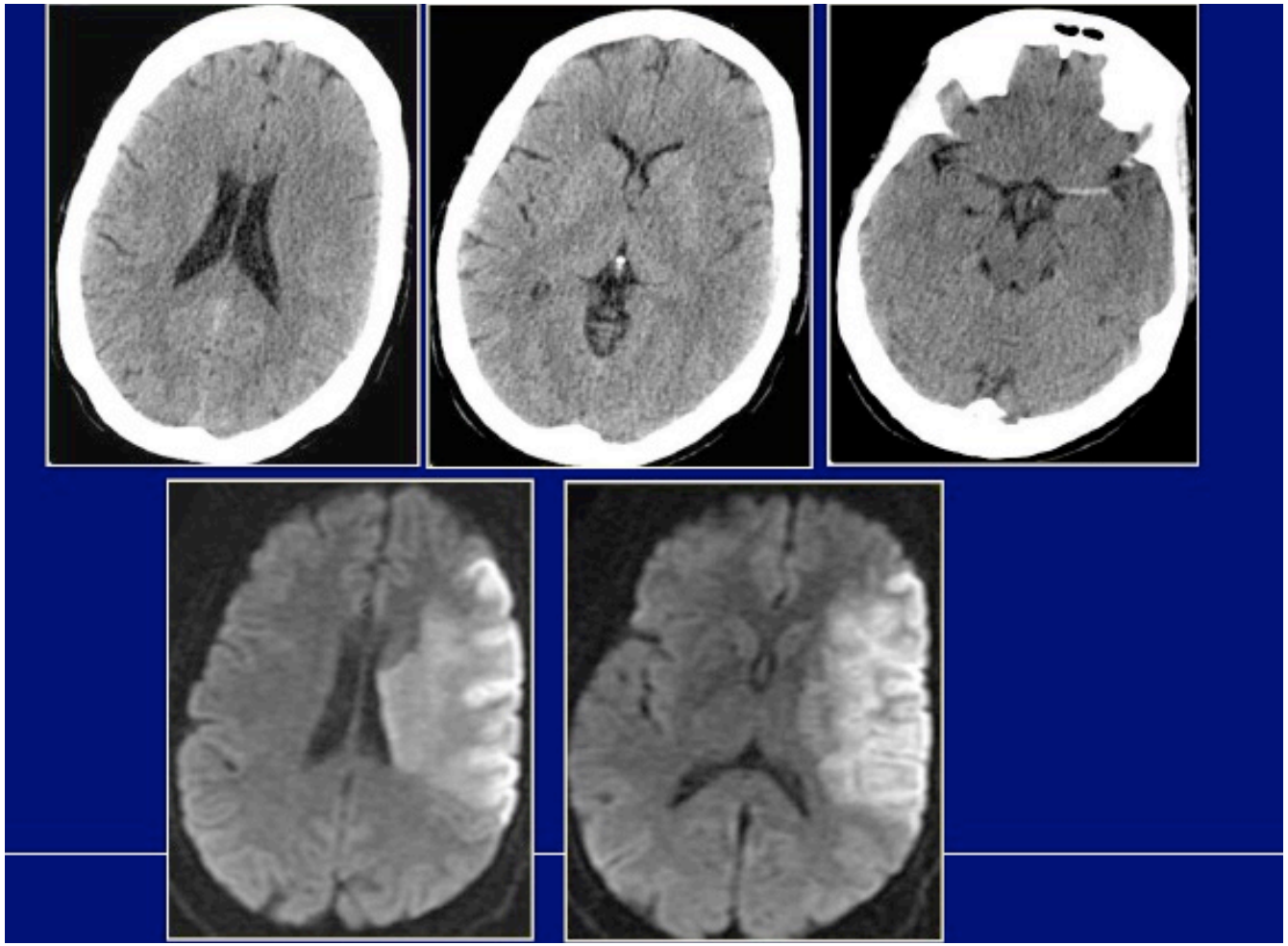
Fibrinolyse en IRM:

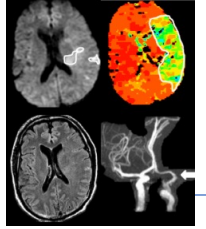
- **Avantages**
  - ✓ Certitude diagnostique
  - ✓ Etendue précise des lésions
  - ✓ Visualisation de l'occlusion artérielle
  - ✓ Visualisation de la « pénombre » ischémique
- **Inconvénients**
  - ✓ Temps d'acquisition plus long
  - ✓ Impossible chez certains patients
  - ✓ Pas de critères validés pour les contre-indications
  - ✓ Peut compliquer la décision (microsaignements, lésion étendue en diffusion, absence d'occlusion...)



Fibrinolyse cérébrale:
Quelle imagerie initiale

Fibrinolyse en IRM: Intérêt pour le diagnostic positif de l'AVCI





Fibrinolyse cérébrale:
Quelle imagerie initiale

Fibrinolyse en IRM: Protocole IRM

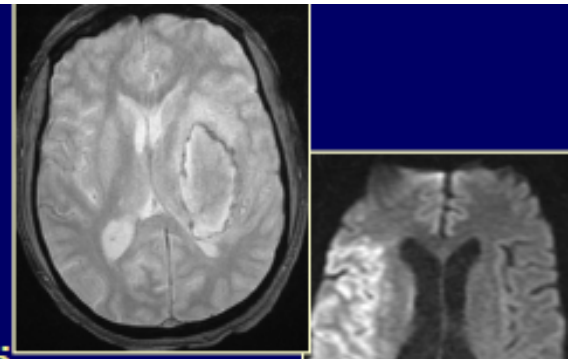
- Axial T2* 2mn
- Axial Diffusion 1mn
- Axial FLAIR 2mn50
- ARM Willis 3DTOF 2mn50

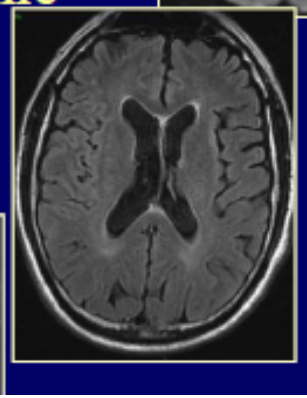
Hématome

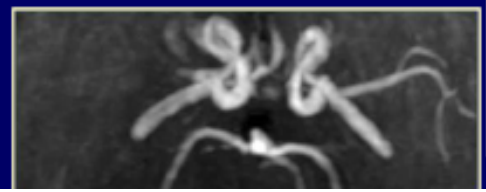
Ischémie aiguë

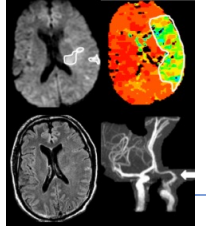
Datation de l'ischémie

Occlusion artérielle



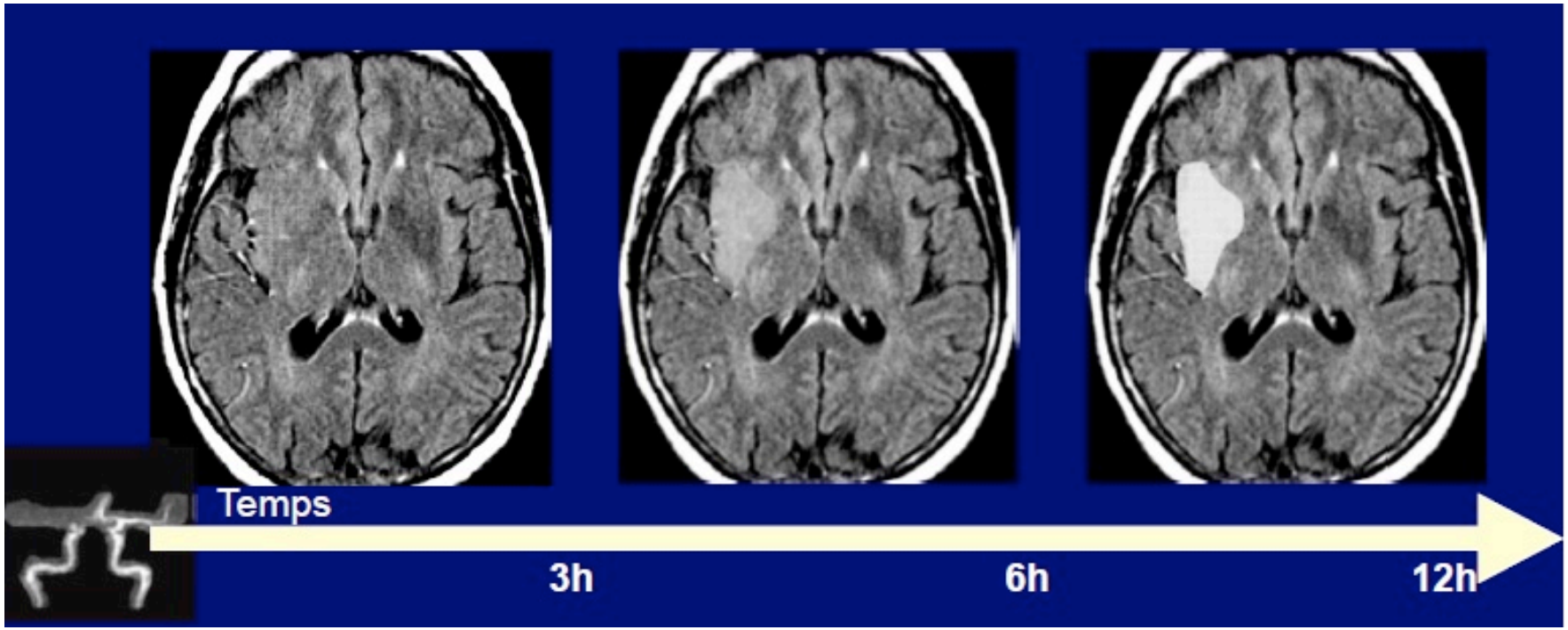


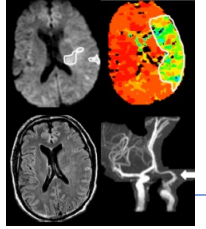




Fibrinolyse cérébrale:
Quelle imagerie initiale

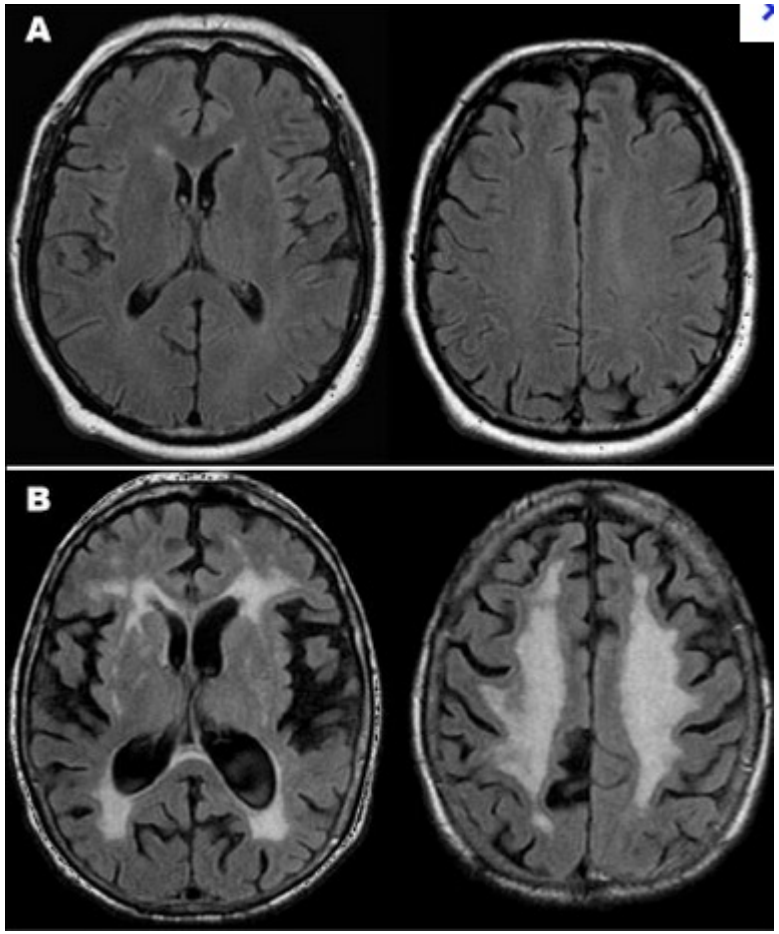
Fibrinolyse en IRM: FLAIR un outils de datation?



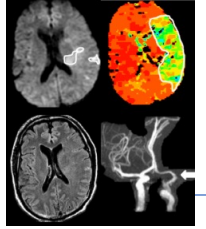


Fibrinolyse cérébrale:
Quelle imagerie initiale

<u>Fibrinolyse en IRM:</u> une multitude d'information!!!

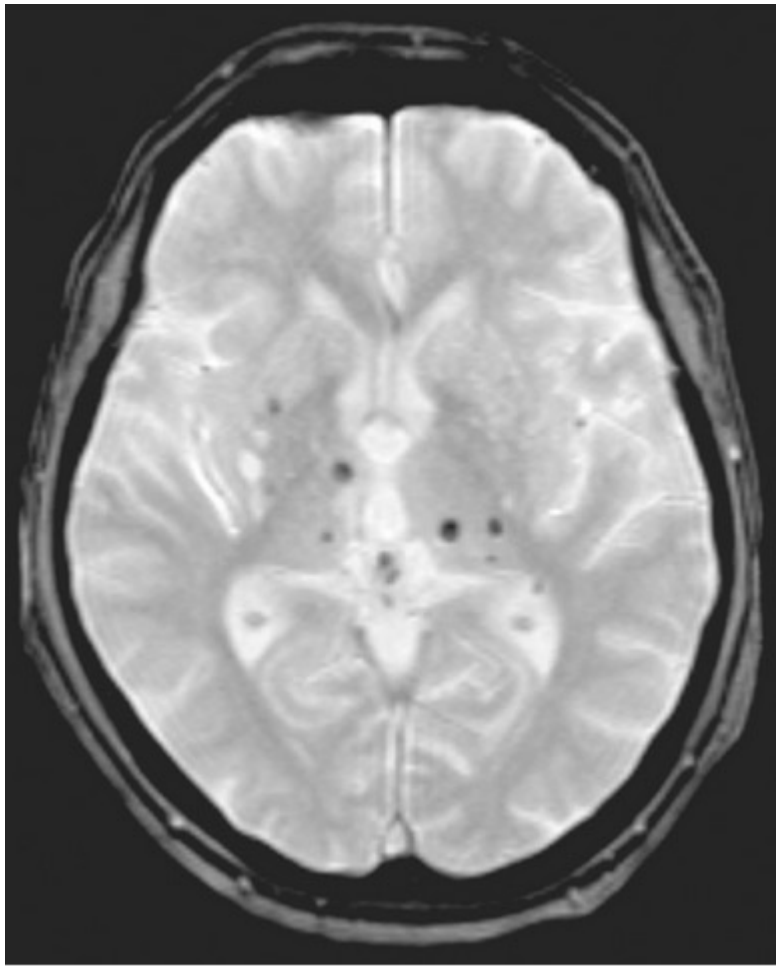


← Détection d'une leucoaraïose évoluée. CI au rtPA?

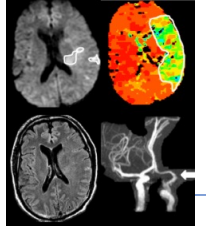


Fibrinolyse cérébrale:
Quelle imagerie initiale

Fibrinolyse en IRM: une multitude d'information!!!



← Microbleeds en T2*. CI au rtPA?

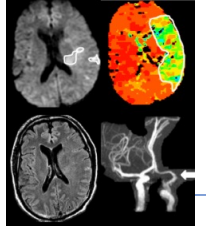


Fibrinolyse cérébrale:
Quelle imagerie initiale

Fibrinolyse en TDM:

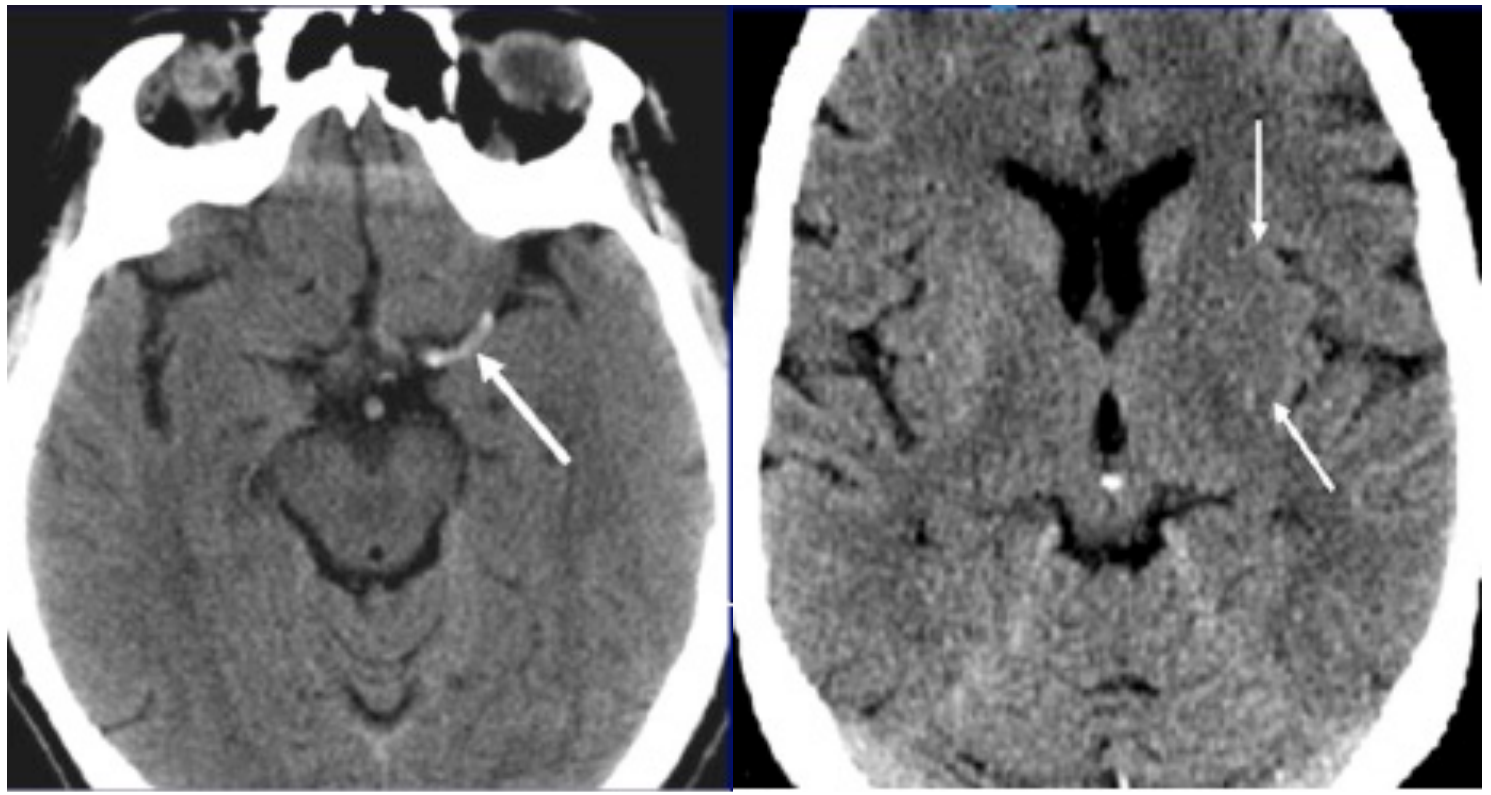
- Signes précoces >33% ACM associés à mortalité et hémorragies intracrâniennes dans groupe t-PA (ECASS I)

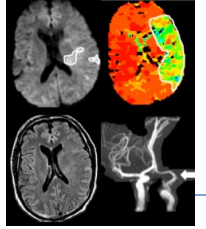
- Mais,
  - ✓ Reproductibilité mauvaise
  - ✓ Pas extrapolable à la fenêtre 0-3H
  - ✓ Pas d'interaction avec bénéfice dans ECASS II et NINDS



Fibrinolyse cérébrale:
Quelle imagerie initiale

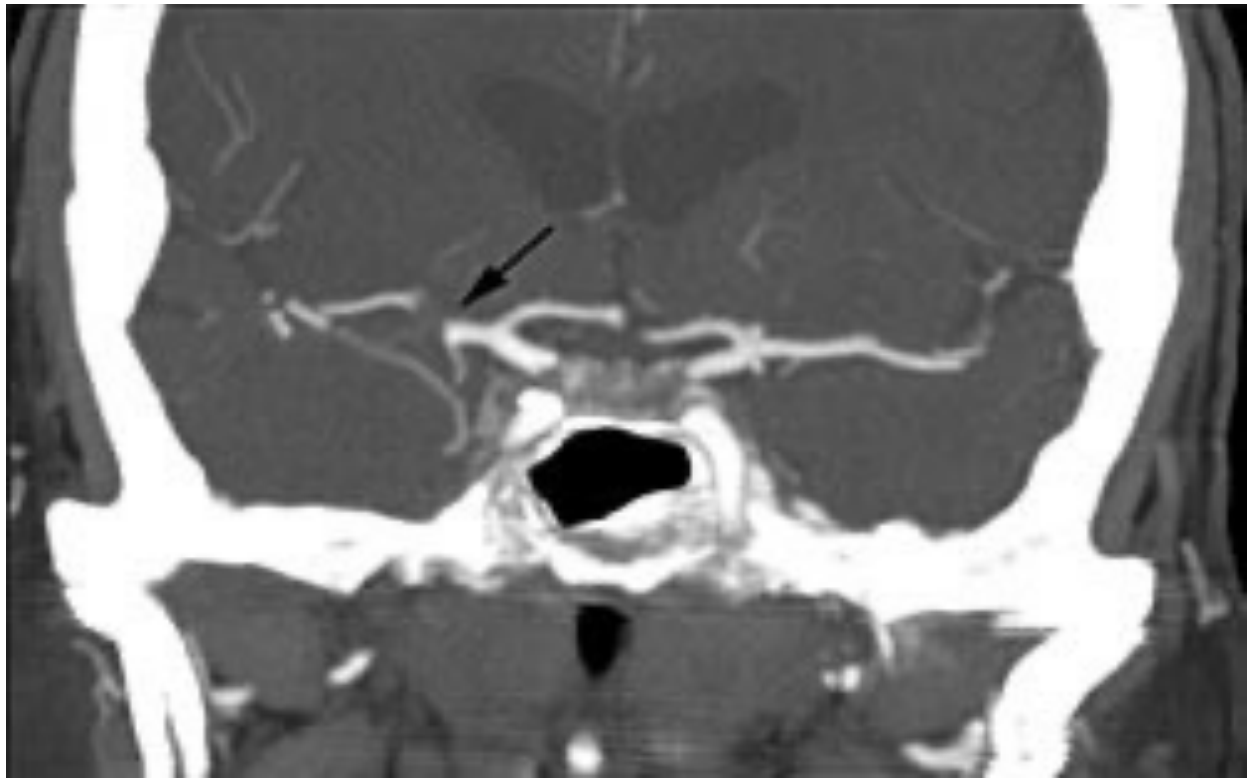
Fibrinolyse en TDM: Signes précoces



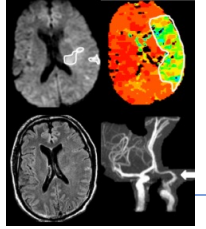


Fibrinolyse cérébrale:
Quelle imagerie initiale

<u>Fibrinolyse en TDM:</u> Angio-TDM TSAO une aide au diagnostic

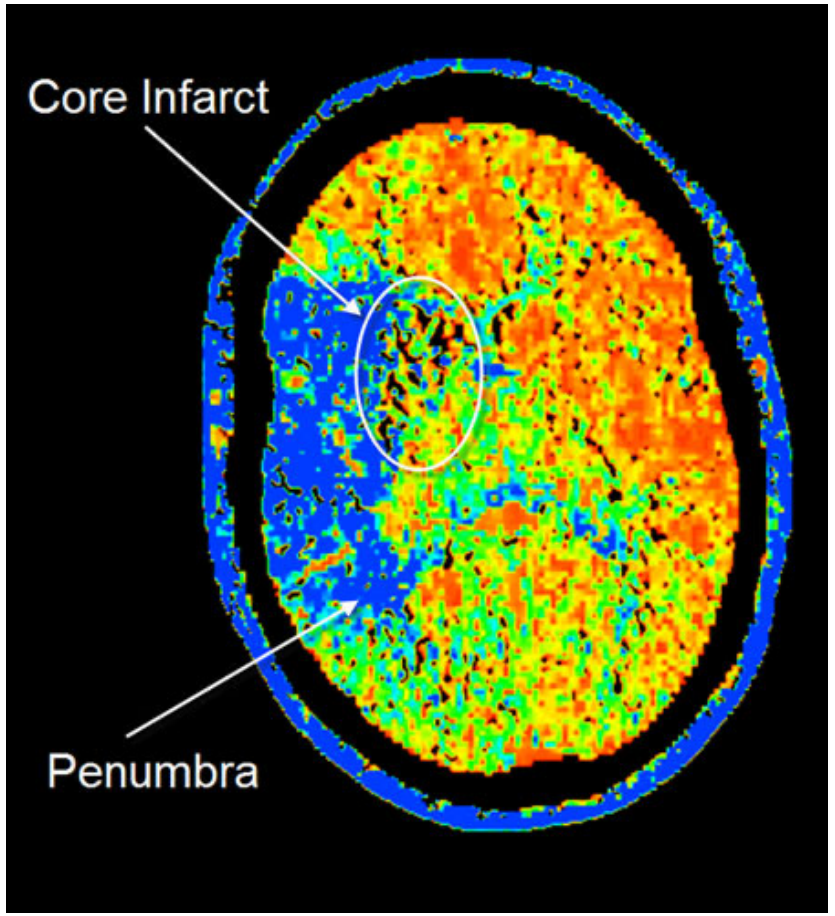


↑ Confirmation angioTDM d'une occlusion symptomatique

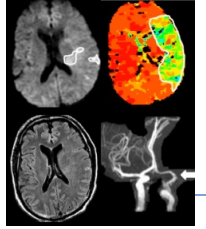


Fibrinolyse cérébrale:
Quelle imagerie initiale

Fibrinolyse en TDM: TDM de perfusion



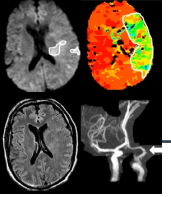
↑ Confirmation par scanner de perfusion d'une occlusion symptomatique



Fibrinolyse cérébrale:
En pratique

Contre-indications (SFNV):

- Le scanner ou l'IRM montre une hémorragie ou un effet de masse (secondaire à une tumeur, une malformation artérioveineuse ou autre)
- Traitement anticoagulant oral en cours ou INR > 1,7
- Un traitement par héparine (ou HBPM à dose efficace) a été administré au cours des 48 heures précédant l'accident ischémique cérébral et le TCA (ou l'activité anti-Xa) est allongé.
- Taux des plaquettes < 100 000/mm^3
- Autre AVC ou tout traumatisme crânien sévère dans les 3 mois précédents
- Pression artérielle systolique > 185 mmHg ou pression artérielle diastolique > 110 mmHg au moment de l'administration du rt-PA
- Déficit neurologique en voie de régression
- Déficit neurologique mineur (NIHSS < 4, tel que déficit sensitif isolé, dysarthrie isolée ou déficit moteur minime)
- Antécédents d'hémorragie intracrânienne, de malformation artérioveineuse ou d'anévrisme intracérébral
- Le patient présente un syndrome méningé (même si le scanner cérébral est normal)
- Glycémie < 0,5 g/L ou > 4 g/L
- Crise d'épilepsie lors de l'installation de l'accident ischémique cérébral*
- Intervention chirurgicale majeure < 14 jours
- Infarctus du myocarde récent (moins de 3 semaines)
- Ponction lombaire ou ponction récente d'un vaisseau non compressible (moins d'une semaine)
- Score du NIHSS > 25 ou coma profond, avec déviation forcée des yeux et hémiplégie complète
- Le scanner ou l'IRM cérébrale montre des signes étendus d'ischémie (atténuation de densité ou effet de masse > 1/3 du territoire de l'artère cérébrale moyenne)
- Endocardite infectieuse
- Antécédents de péricardite datant de moins de 3 mois
- Refus du patient et de sa famille
- Femmes enceintes ou en *post-partum* < 14 jours
- Handicap neurologique préexistant (dépendant, non ambulatoire)
- Le patient présente une dissection intracrânienne
- Le rapport bénéfice-risque du rt-PA doit être soigneusement évalué chez les patients de plus de 80 ans



TIV et AOD

American Heart Association | American Stroke Association
life is why

Thrombin inhibitors or factor Xa inhibitors	The use of IV alteplase in patients taking direct thrombin inhibitors or direct factor Xa inhibitors has not been firmly established but may be harmful.† (*Class III: Harm; LOE C-EO*)‡§ IV alteplase should not be administered to patients taking direct thrombin inhibitors or direct factor Xa inhibitors unless laboratory tests such as aPTT, INR, platelet count, ecarin clotting time, thrombin time, or appropriate direct factor Xa activity assays are normal or the patient has not received a dose of these agents for >48 h (assuming normal renal metabolizing function). (Alteplase could be considered when appropriate laboratory tests such as aPTT, INR, ecarin clotting time, thrombin time, or direct factor Xa activity assays are normal or when the patient has not taken a dose of these ACs for >48 h and renal function is normal.)

Anti-II (Thrombine)

Anti-Xa (Xaban)

Pradaxa® dabigatran etexilate

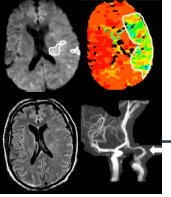
Xarelto® rivaroxaban

Eliquis® apixaban

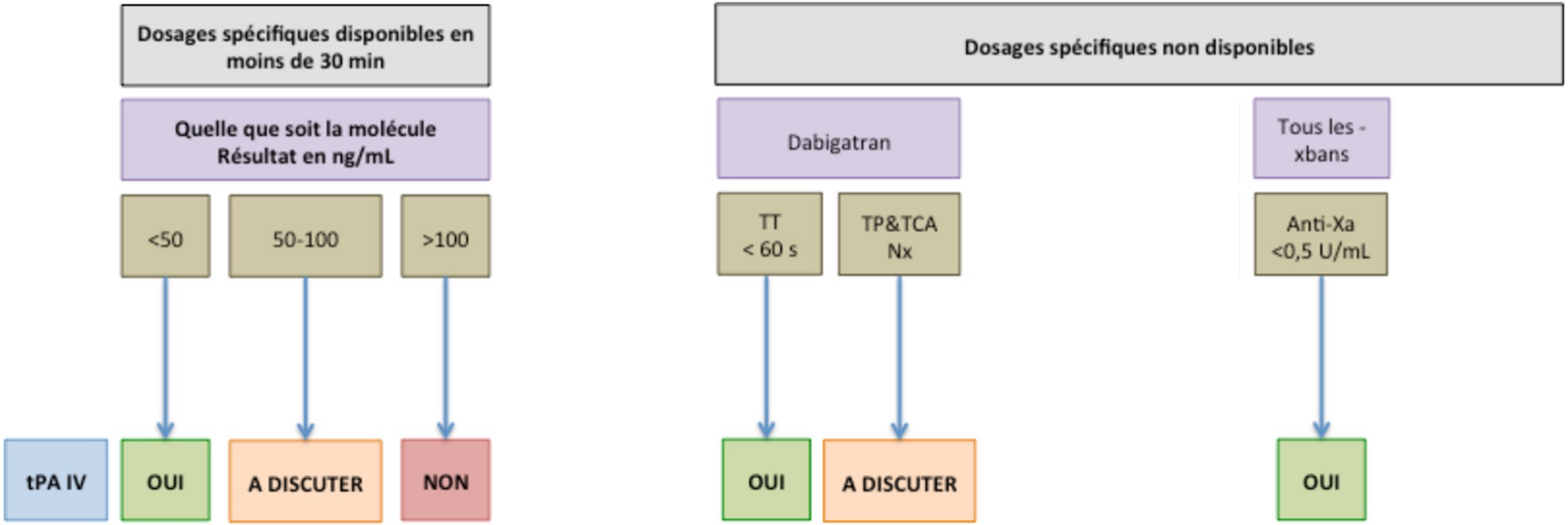
Lixiana® edoxaban

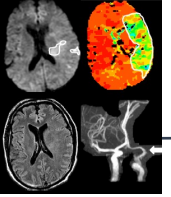
Antidote spécifique

Praxbind® idarucizumab IV INJECTION 5g



TIV et AOD


Dosages spécifiques disponibles en moins de 30 min
Quelle que soit la molécule
Résultat en ng/mL
<50
50-100
>100
tPA IV
OUI
A DISCUTER
NON
Dosages spécifiques non disponibles
Dabigatran
TT
< 60 s
TP&TCA
Nx
OUI
A DISCUTER
Tous les -xbans
Anti-Xa
<0,5 U/mL
OUI



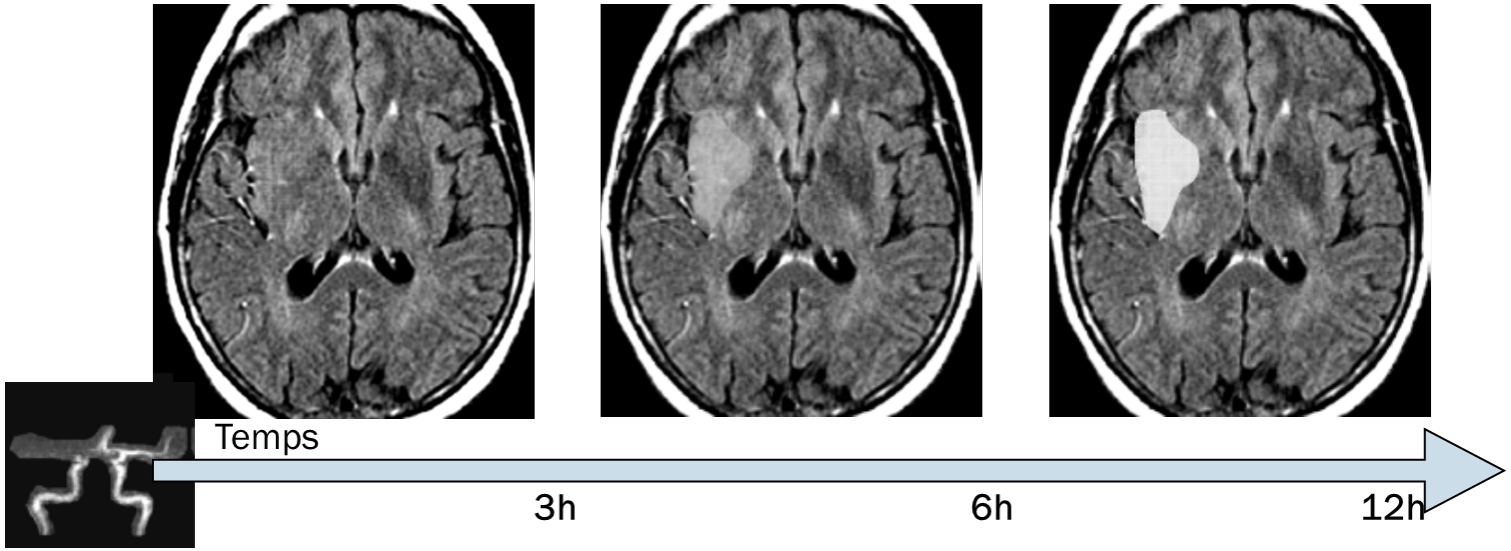
Cas particulier de l'AVC du réveil

The NEW ENGLAND JOURNAL of MEDICINE 2018

ORIGINAL ARTICLE

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

FLAIR (fluid attenuation inversion recovery)



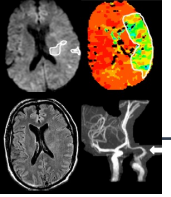
WAKE-UP

Patients:

- 18 et **80 ans autonomes**
- AVCi du réveil ou heure de début inconnue
- Vus bien pour la dernière fois > 4,5 heures
- **IRM:** DWI **+**, FLAIR **–**
- **Exclusion des patients thrombectomisés**

Randomisation:

- Placebo (n=249)
- Alteplase (n=254)



Cas particulier de l'AVC du réveil

Table 2. Primary and Secondary Efficacy Outcomes (Intention-to-Treat Population).*

Outcome	Alteplase Group (N=254)	Placebo Group (N=249)	Effect Variable	Adjusted Value (95% CI)†	P Value
Primary efficacy end point					
Favorable outcome at 90 days — no./total no. (%)‡	131/246 (53.3)	102/244 (41.8)	Odds ratio	1.61 (1.09 to 2.36)	0.02

Table 3. Safety Outcomes.

Outcome	Alteplase Group (N=251)	Placebo Group (N=244)	Adjusted Odds Ratio (95% CI)*	P Value
	no. (%)			
Primary†				
Death or dependency at 90 days	33 (13.5)	44 (18.3)	0.68 (0.39–1.18)	0.17
Death at 90 days	10 (4.1)	3 (1.2)	3.38 (0.92–12.52)	0.07
Secondary				
Symptomatic intracranial hemorrhage				
As defined in SITS-MOST‡	5 (2.0)	1 (0.4)	4.95 (0.57–42.87)	0.15
As defined in ECASS II§	7 (2.8)	3 (1.2)	2.40 (0.60–9.53)	0.21
As defined in ECASS III¶	6 (2.4)	1 (0.4)	6.04 (0.72–50.87)	0.10
As defined in NINDS‖	20 (8.0)	12 (4.9)	1.78 (0.84–3.71)	0.13

WAKE-UP

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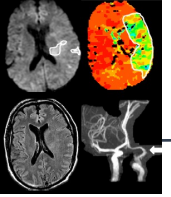


Ténectéplase IV en phase aiguë de l'infarctus cérébral

The NEW ENGLAND JOURNAL of MEDICINE 2012

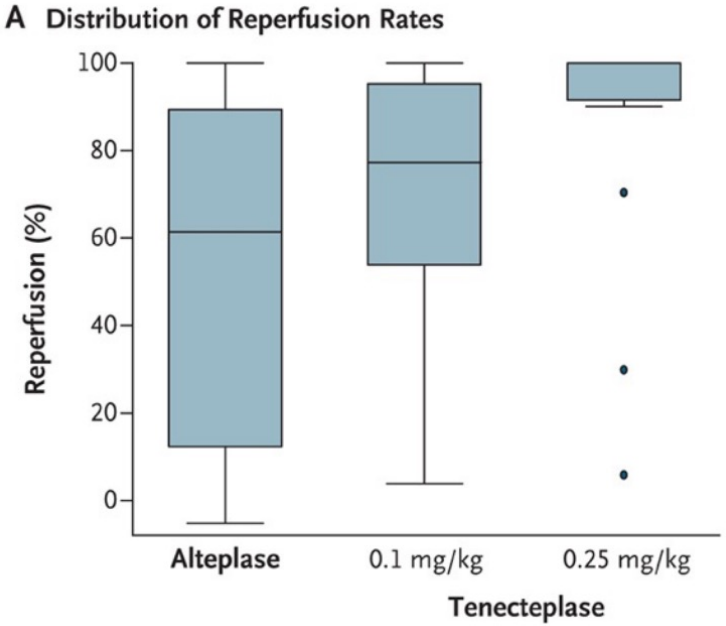
ORIGINAL ARTICLE

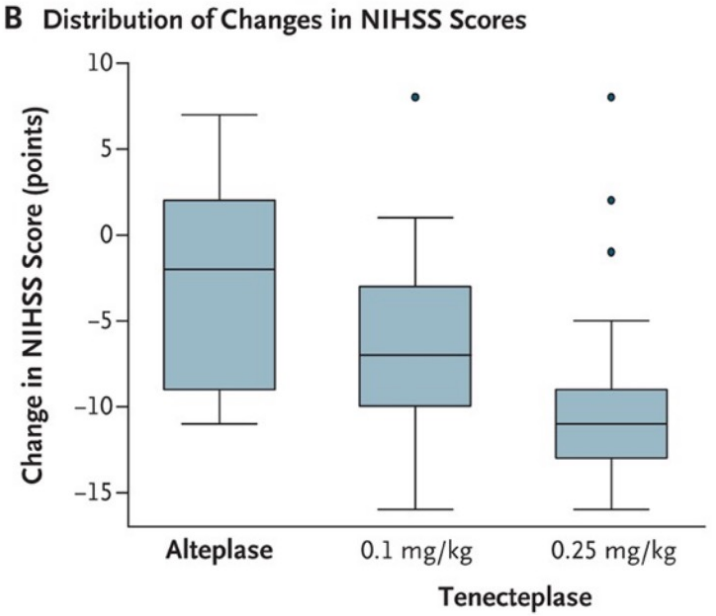
A Randomized Trial of Tenecteplase versus Alteplase for Acute Ischemic Stroke

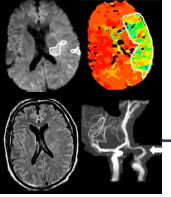
Mark Parsons, M.D., Neil Spratt, M.D., Andrew Bivard, B.Sc., Bruce Campbell, M.D., Kong Chung, M.D., Ferdinand Miteff, M.D., Bill O'Brien, M.D., Christopher Bladin, M.D., Patrick McElduff, Ph.D., Chris Allen, M.D., Grant Bateman, M.D., Geoffrey Donnan, M.D., Stephen Davis, M.D., and Christopher Levi, M.D.

<u>Ténectéplase :</u>

- Forme recombinante rt-PA
- Affinité au fibrinogène +++
- Demi-vie 20 min
- Injection en bolus

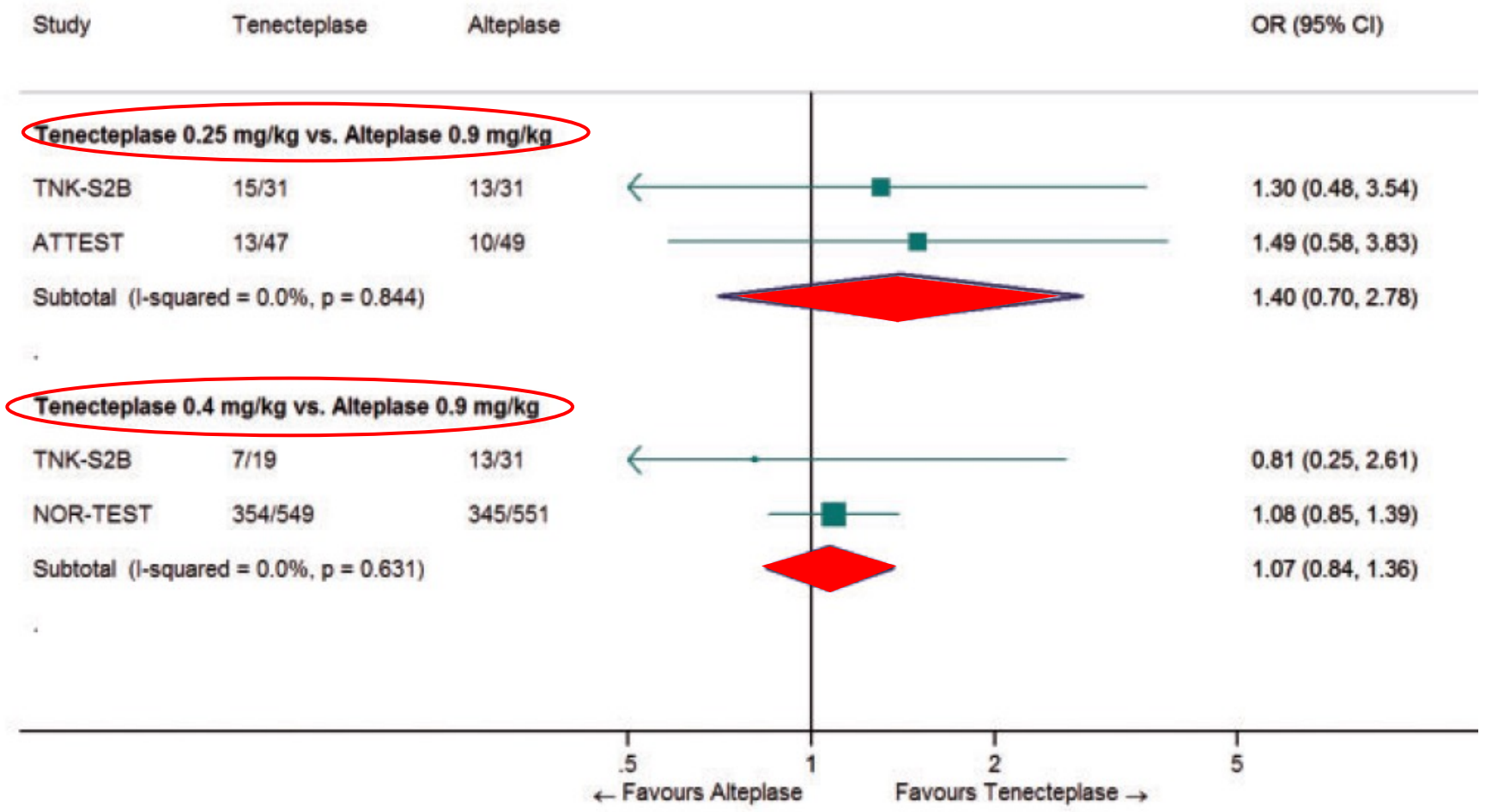




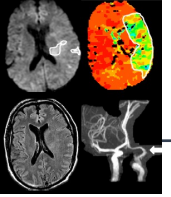


Ténectéplase IV en phase aiguë de l'infarctus cérébral

Patients non éligibles à la thrombectomie - Efficacité mRS[0-1]

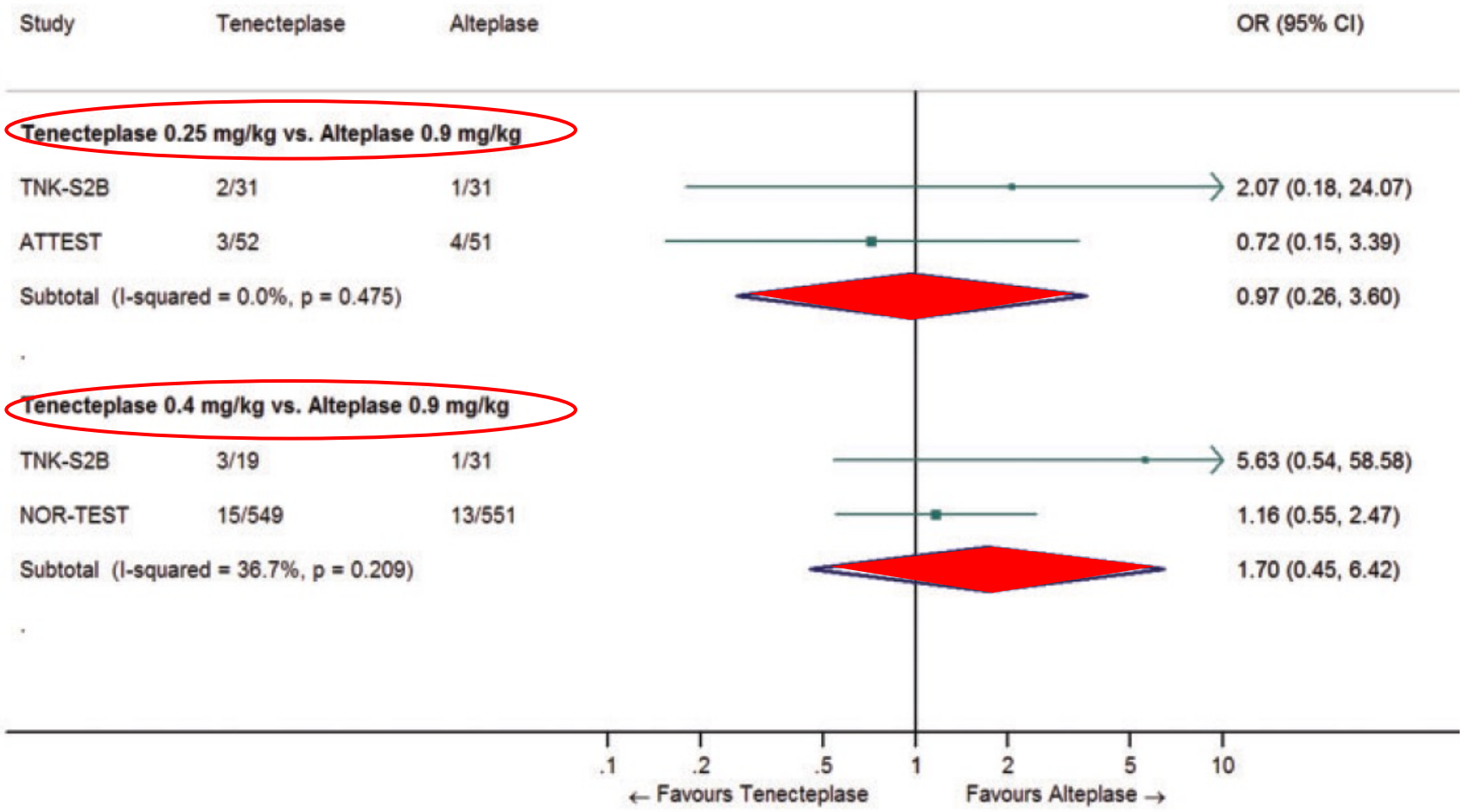


Berge *et al.* **European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke.** *European Stroke Journal* 2021



Ténectéplase IV en phase aiguë de l'infarctus cérébral

Patients non éligibles à la thrombectomie – Sécurité sICH



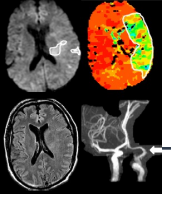
ESO
EUROPEAN STROKE ORGANISATION

For patients with acute ischaemic stroke of <4.5 h duration and not eligible for thrombectomy, we suggest intravenous thrombolysis with alteplase over intravenous thrombolysis with tenecteplase. Please see paragraph 5.2 for patients eligible for mechanical thrombectomy.

Quality of evidence: **Low** ⊕⊕

Strength of recommendation: **Weak** ↑?

Berge *et al.* **European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke.** *European Stroke Journal* 2021



Ténectéplase IV en phase aiguë de l'infarctus cérébral

Tenecteplase vs. Alteplase before Stroke Thrombectomy

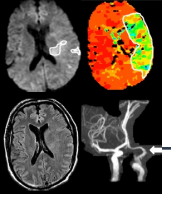
MULTICENTER, RANDOMIZED, OPEN-LABEL TRIAL WITHIN 4.5 HOURS AFTER ISCHEMIC STROKE

N=101 0.25 mg/kg Tenecteplase		N=101 Alteplase
22% P=0.03 (superiority) P=0.002 (noninferiority)	Reperfusion >50% at prethrombectomy angiogram	10%
2 P=0.04	90-Day Functional Outcome NO SYMPTOMS 0 1 2 3 4 5 6 DEATH Median Modified Rankin Score	3

No Significant Difference in Adverse Events

The NEW ENGLAND JOURNAL of MEDICINE

Campbell et al. 2018

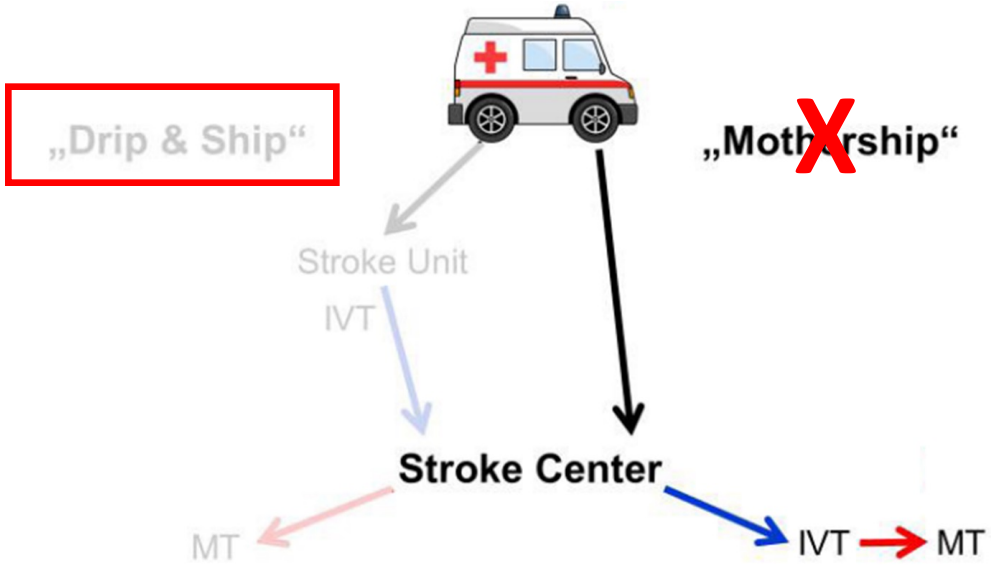


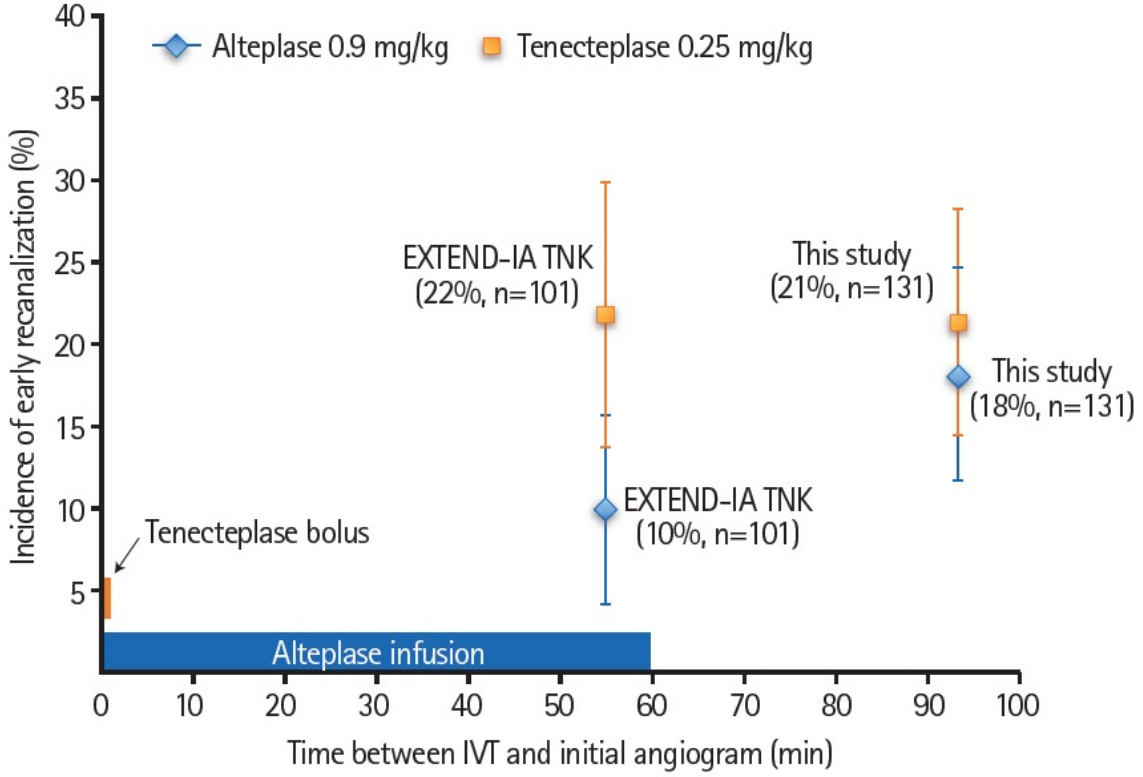
Ténectéplase IV en phase aiguë de l'infarctus cérébral

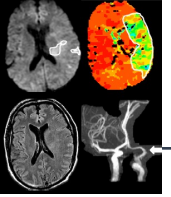
JoS JOURNAL OF STROKE

Recanalization before Thrombectomy in Tenecteplase vs. Alteplase–Treated Drip–and–Ship Patients

Pierre Seners,[a] Jildaz Caroff,[b,*] Nicolas Chausson,[c,*] Guillaume Turc,[a] Christian Denier,[d] Michel Piotin,[e] Manvel Aghasaryan,[c] Cosmin Alecu,[c] Olivier Chassin,[d] Bertrand Lapergue,[f] Olivier Naggara,[g] Marc Ferrigno,[h] Caroline Arquizan,[i] Tae-Hee Cho,[j] Ana-Paula Narata,[k] Sébastien Richard,[l] Nicolas Bricout,[m] Mikaël Mazighi,[e] Vincent Costalat,[n] Benjamin Gory,[o] Séverine Debiais,[p] Arturo Consoli,[q] Serge Bracard,[o] Catherine Oppenheim,[g] Jean-Louis Mas,[a] Didier Smadja,[c,†] Laurent Spelle,[b,†] Jean-Claude Baron,[a,†] on behalf of the PREDICT-RECANAL collaborators







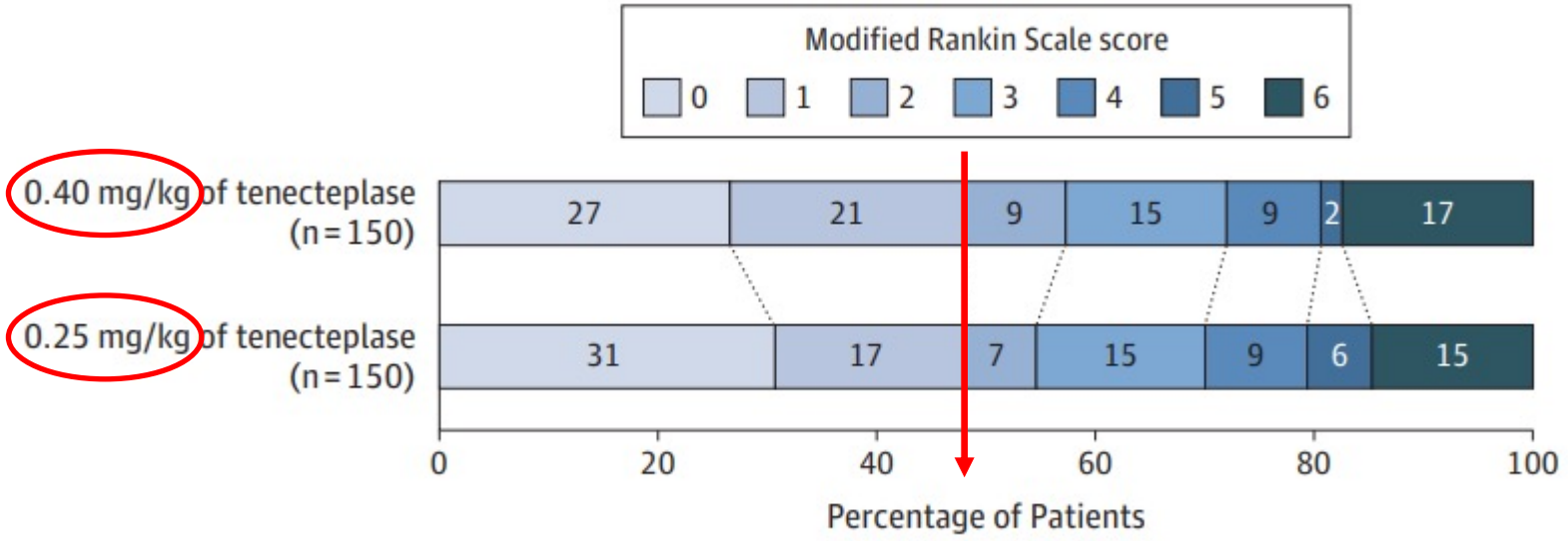
Ténectéplase IV en phase aiguë de l'infarctus cérébral

2020

JAMA | Original Investigation

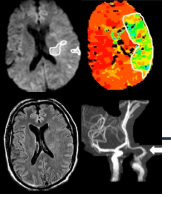
Effect of Intravenous Tenecteplase Dose on Cerebral Reperfusion Before Thrombectomy in Patients With Large Vessel Occlusion Ischemic Stroke

The EXTEND-IA TNK Part 2 Randomized Clinical Trial

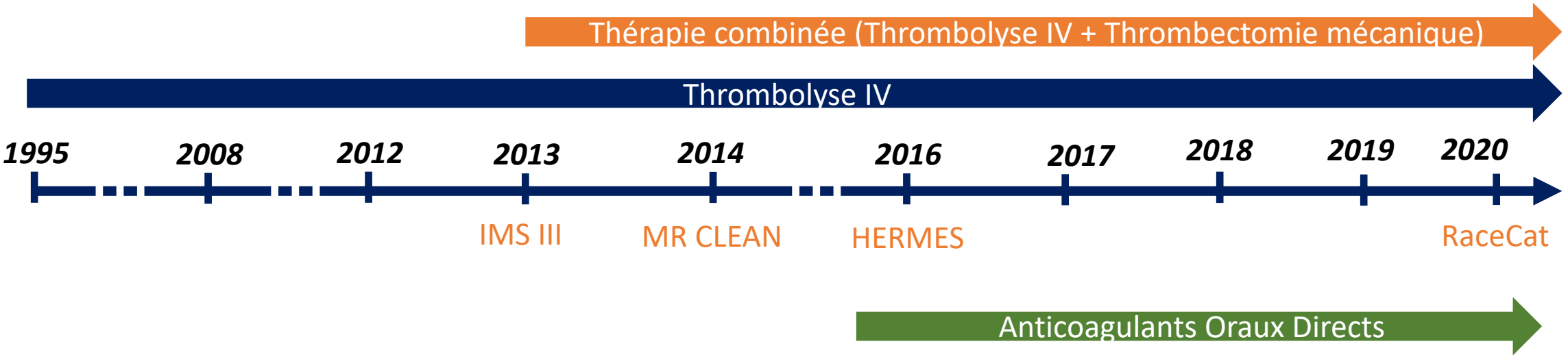


ESO EUROPEAN STROKE ORGANISATION

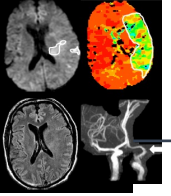
For patients with acute ischaemic stroke of < 4.5 h duration and with large vessel occlusion who are candidates for mechanical thrombectomy and for whom intravenous thrombolysis is considered before thrombectomy, we suggest intravenous thrombolysis with tenecteplase 0.25 mg/kg over intravenous thrombolysis with alteplase 0.9 mg/kg.
Quality of evidence: **Low** ⊕⊕
Strength of recommendation: **Weak** ↑?



La thérapie combinée



Les leçons des premiers essais négatifs

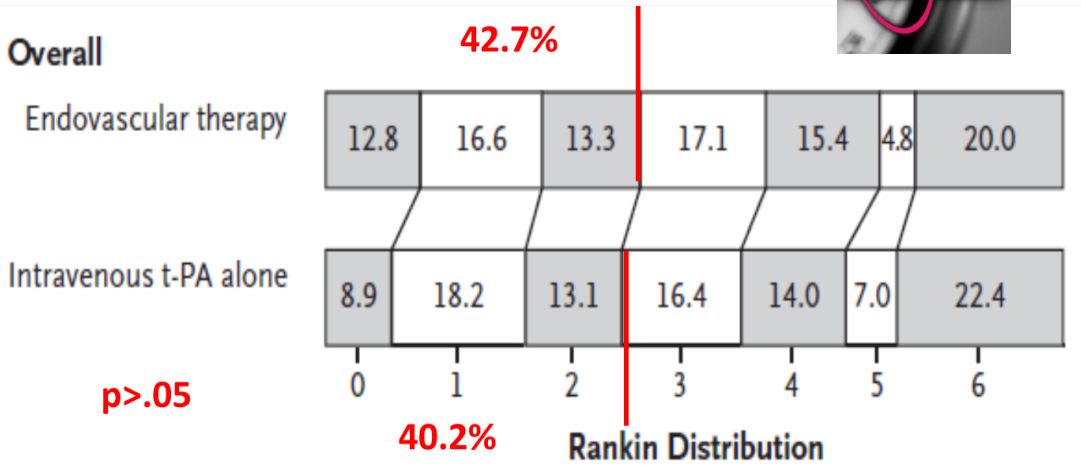


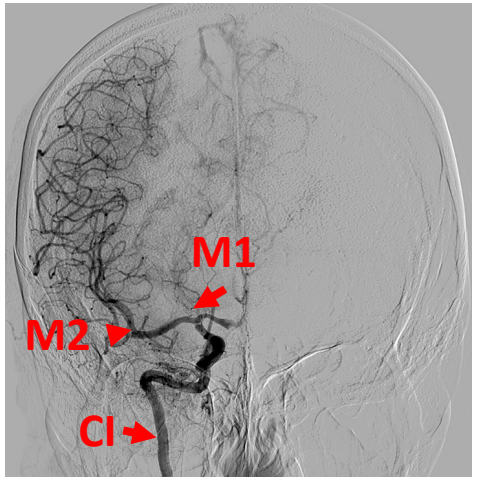
The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL

Endovascular Treatment for Acute Ischemic Stroke — Still Unproven

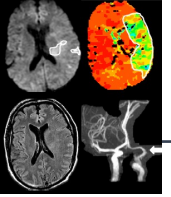
Marc I. Chimowitz, M.B., Ch.B.





		rt-PA seul	rt-PA + thrombectomie	
n		69/222	147/434	
CI		35%	84%	+ 49%
M1		68%	86%	+ 18%
M2		77%	88%	+ 11%

Broderick JP, *et al.* **Endovascular therapy after intravenous t-PA versus t-PA alone for stroke.** *N Engl J Med*. 2013.



2015: Entrée dans l'ère de la thrombectomie mécanique

www.mrclean-trial.org

MR CLEAN

A Multicenter Randomized CLinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands

- AVC ischémiques (n=500)
- AngioTDM TSAO, IRM/ARM
- Occlusion proximale (CI et/ou ACM M1-M2)
- rt-PA IV

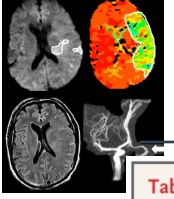
n=267

n=233

+

J90: Score de Rankin modifié (mRS)

Berkhemer OA *et al.* **A randomized trial of intraarterial treatment for acute ischemic stroke**. *N Engl J Med.* 2015

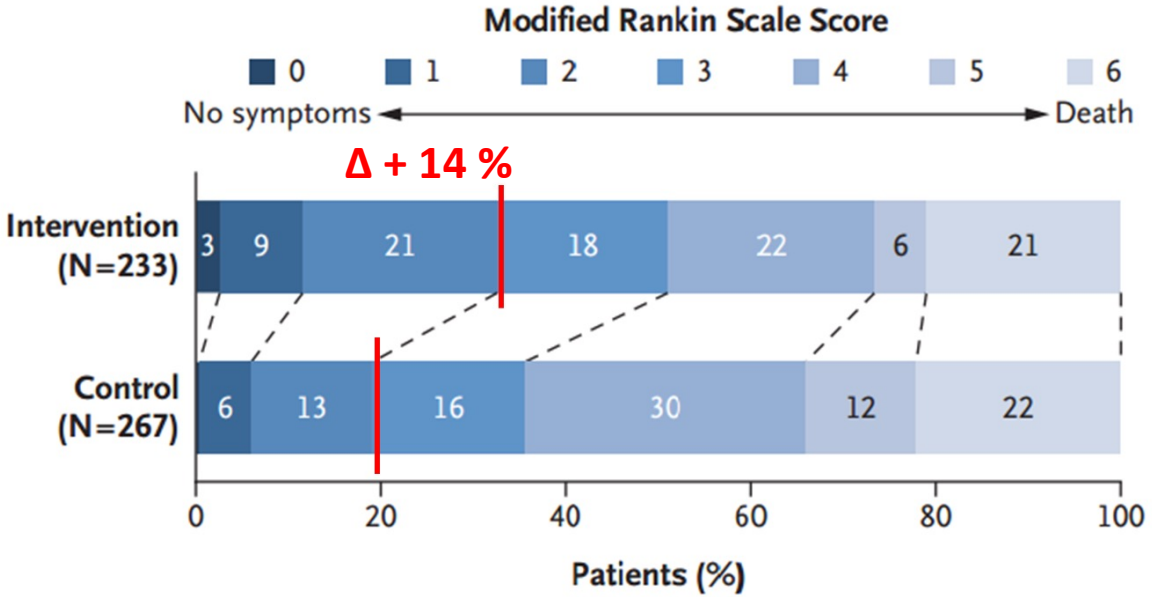


MR CLEAN: Preuve de l'efficacité de la thérapie combinée

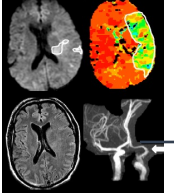
MR CLEAN
www.mrclean-trial.org
A Multicenter Randomized CLinical trial of Endovascular treatment for Acute ischemic stroke in the Netherlands

Table 1. Baseline Characteristics of the 500 Patients.*

Characteristic	Intervention (N=233)	Control (N=267)
Age — yr		
Median	65.8	65.7
Interquartile range	54.5–76.0	55.5–76.4
Male sex — no. (%)	135 (57.9)	157 (58.8)
NIHSS score†		
Median (interquartile range)	17 (14–21)	18 (14–22)
Range	3–30	4–38
Location of stroke in left hemisphere — no. (%)	116 (49.8)	153 (57.3)
History of ischemic stroke — no. (%)	29 (12.4)	25 (9.4)
Atrial fibrillation — no. (%)	66 (28.3)	69 (25.8)
Diabetes mellitus — no. (%)	34 (14.6)	34 (12.7)
Prestroke modified Rankin scale score — no. (%)‡		
0	190 (81.5)	214 (80.1)
1	21 (9.0)	29 (10.9)
2	12 (5.2)	13 (4.9)
>2	10 (4.3)	11 (4.1)
Systolic blood pressure — mm Hg§	146±26.0	145±24.4
Treatment with IV alteplase — no. (%)	203 (87.1)	242 (90.6)
Time from stroke onset to start of IV alteplase — min		
Median	85	87
Interquartile range	67–110	65–116
ASPECTS — median (interquartile range)¶	9 (7–10)	9 (8–10)
Intracranial arterial occlusion — no./total no. (%)‖		
Intracranial ICA	1/233 (0.4)	3/266 (1.1)
ICA with involvement of the M1 middle cerebral artery segment	59/233 (25.3)	75/266 (28.2)
M1 middle cerebral artery segment	154/233 (66.1)	165/266 (62.0)
M2 middle cerebral artery segment	18/233 (7.7)	21/266 (7.9)
A1 or A2 anterior cerebral artery segment	1/233 (0.4)	2/266 (0.8)
Extracranial ICA occlusion — no./total no. (%)‖**	75/233 (32.2)	70/266 (26.3)
Time from stroke onset to randomization — min††		
Median	204	196
Interquartile range	152–251	149–266
Time from stroke onset to groin puncture — min		
Median	260	NA
Interquartile range	210–313	

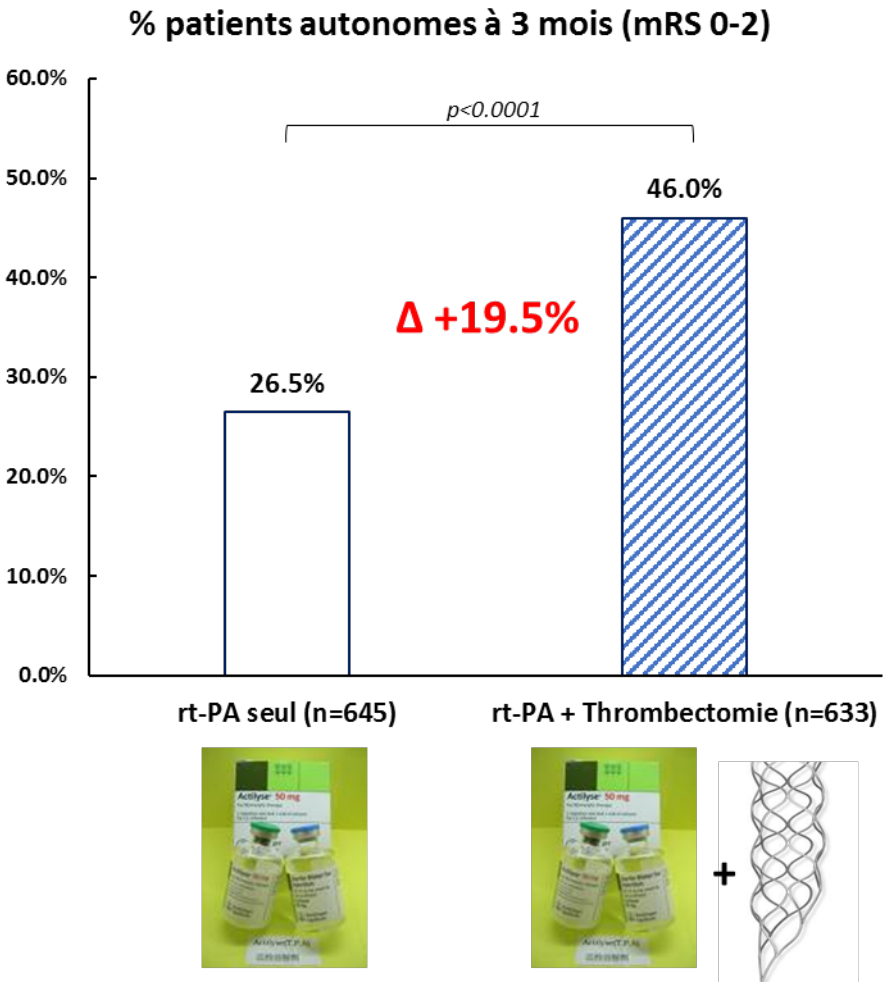


Berkhemer OA *et al.* **A randomized trial of intraarterial treatment for acute ischemic stroke**. *N Engl J Med.* 2015



Méta-analyse HERMES confirme l'efficacité de la thérapie combinée

Pool de 5 études : MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA

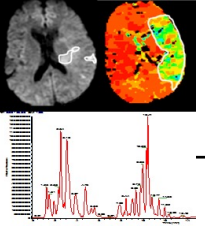


	Intervention population	Control population	Risk difference (%)	Rate ratio (95% CI)	Odds ratio (95% CI)	Adjusted rate ratio (95% CI)	Adjusted odds ratio (95% CI)
Symptomatic intracranial haemorrhage	4·4% (28/634)	4·3% (28/653)	0·1	1·06 (0·63–1·80); p=0·82	1·07 (0·62–1·83); p=0·81	1·07 (0·62–1·80); p=0·81	1·07 (0·62–1·84); p=0·81
Parenchymal haematoma type 2	5·1% (32/629)	5·3% (34/641)	−0·2	0·99 (0·61–1·61); p=0·97	0·99 (0·60–1·63); p=0·97	1·04 (0·64–1·69); p=0·88	1·04 (0·63–1·72); p=0·88
Mortality	15·3% (97/633)	18·9% (122/646)	−3·6	0·82 (0·63–1·07); p=0·15	0·77 (0·54–1·10); p=0·16	0·82 (0·62–1·08); p=0·15	0·73 (0·47–1·13); p=0·16

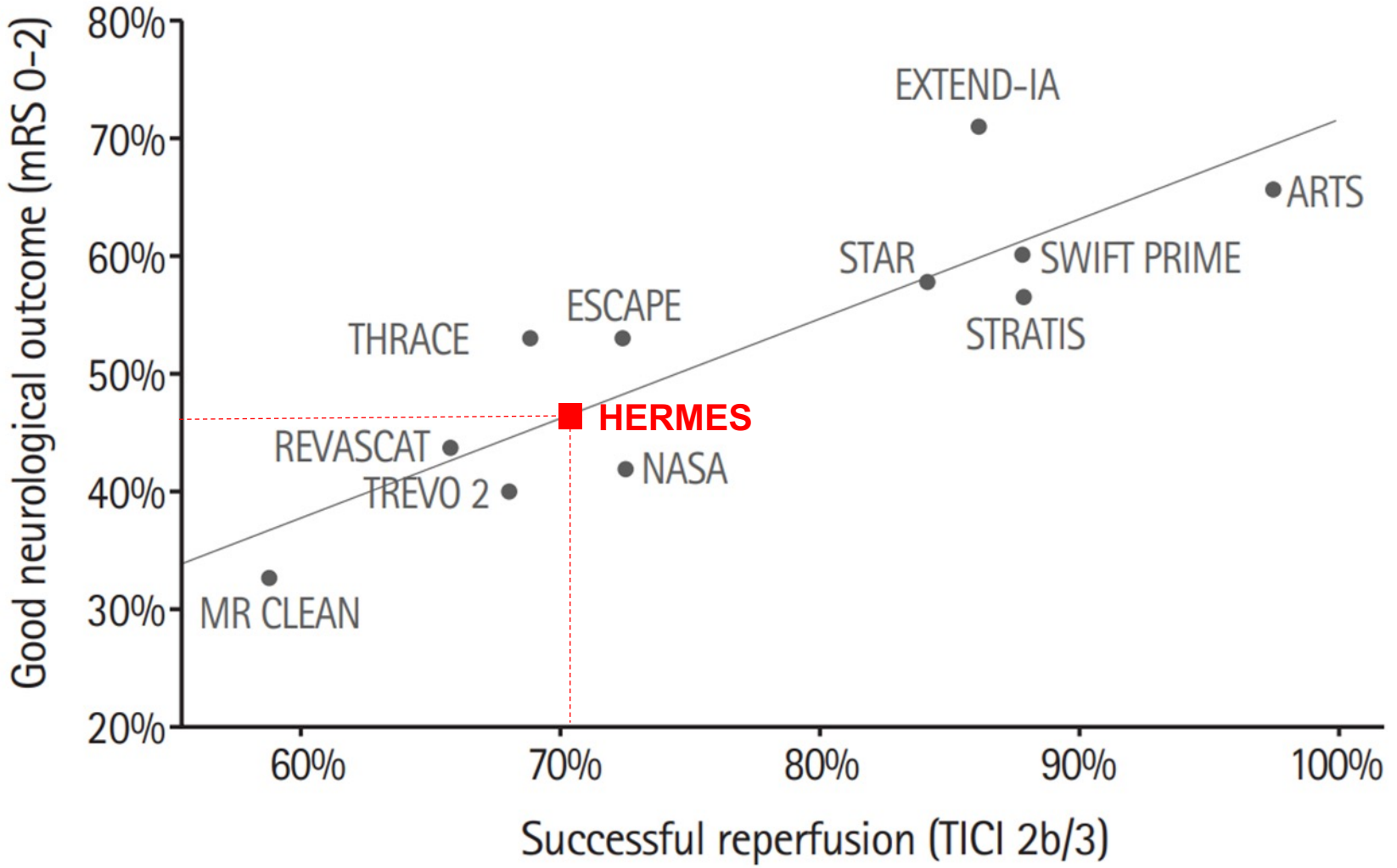
Data show the proportion of patients with outcome (n/N), unless otherwise stated.

Table 4: Safety outcomes at 90 days

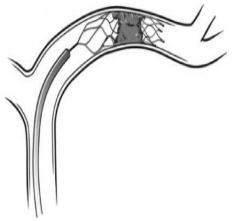
Goyal M, *et al.* **Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials.** *Lancet.* 2016



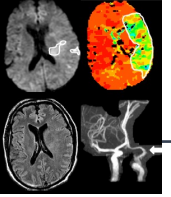
Relation linéaire entre reperfusion et pronostic clinique à 3 mois



+



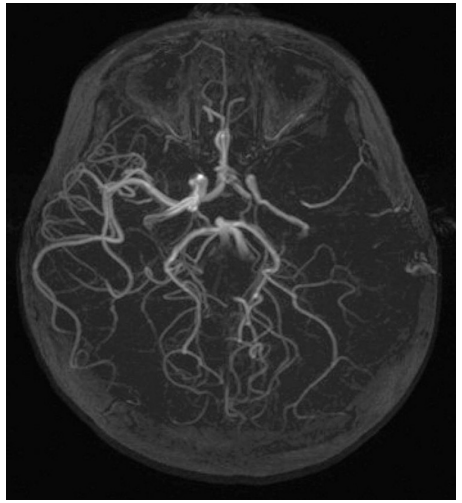
Andersson T *et al.* **The Aspirations of Direct Aspiration for Thrombectomy in Ischemic Stroke: A Critical Analysis**. *J Stroke.* **2019.**



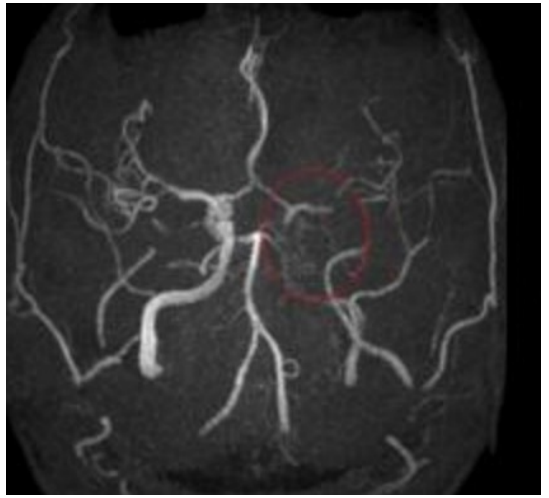
Thérapie combinée: Gold Standard de l'occlusion proximale

La TM est recommandée en complément de la thrombolyse systémique chez les patients présentant une occlusion proximale des artères de la circulation antérieure **(Grade A).**

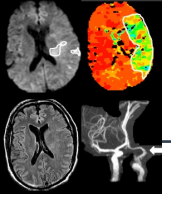
Occlusion de l'ACM M1-M2



Occlusion carotido-sylvienne



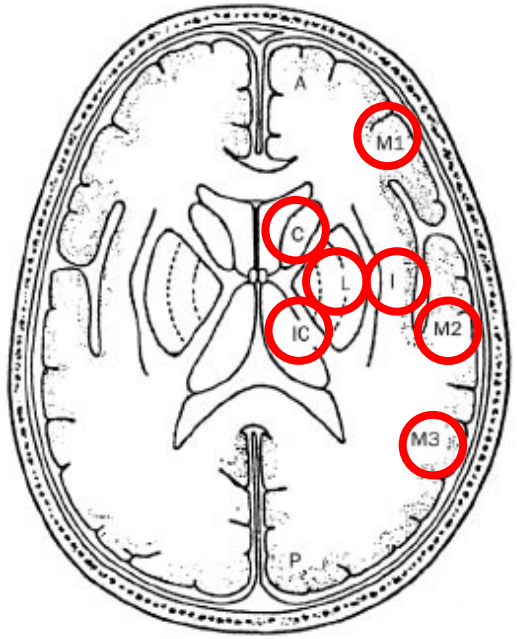
- L'occlusion artérielle doit être confirmée par une imagerie vasculaire (ARM 3DTOF ou gado; angioTDM TSAO) avant d'envisager la TM **(Grade A).**

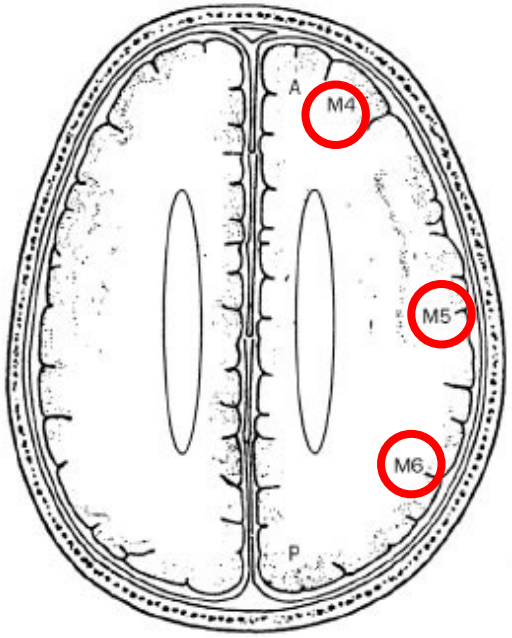


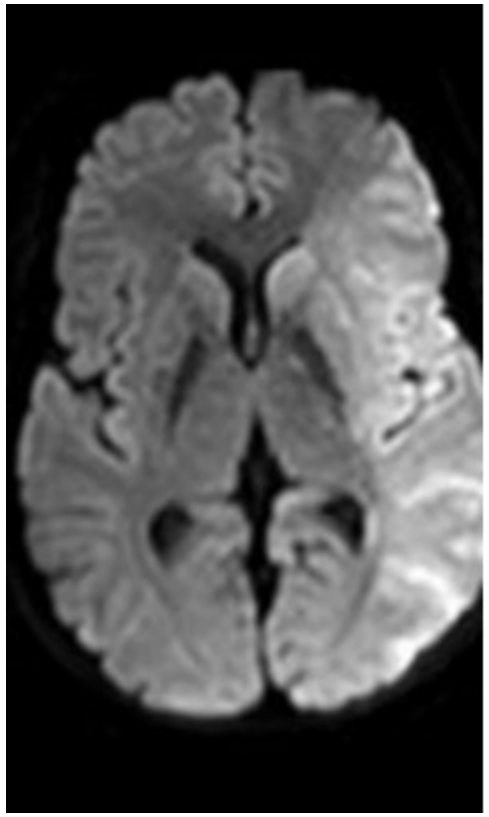
Thérapie combinée: Gold Standard de l'occlusion proximale

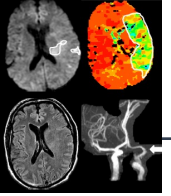
La TM pourra être contre-indiquée en cas de lésions ischémiques massives en DWI **(Grade B):**

- ASPECT DWI < 6
- > 2/3 ACM



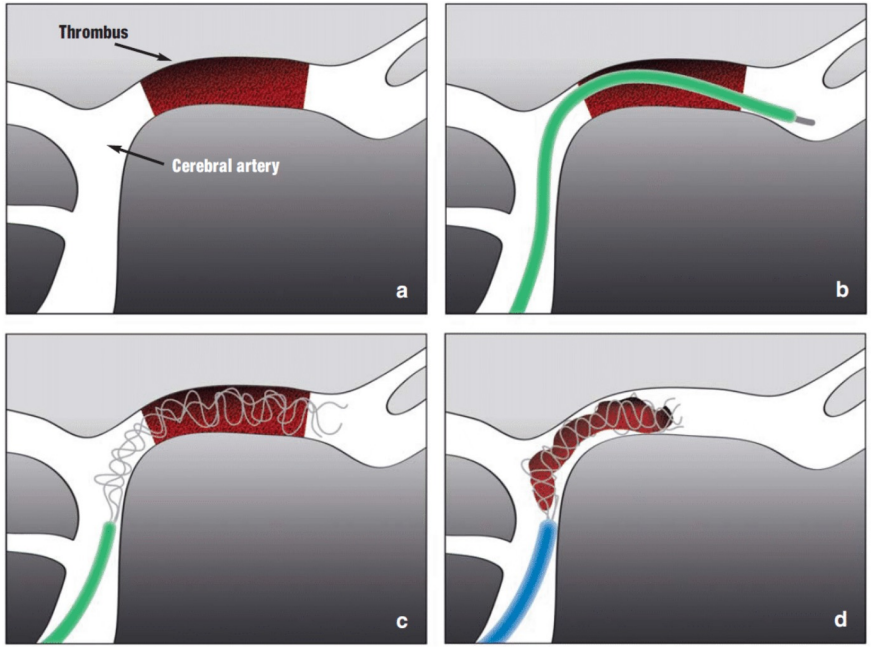


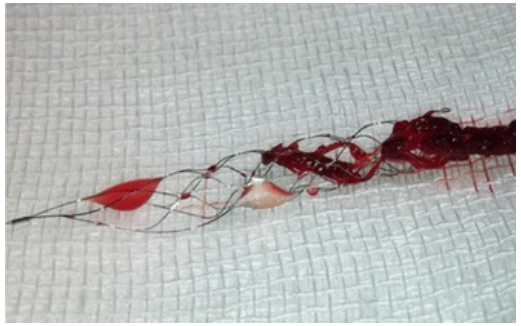




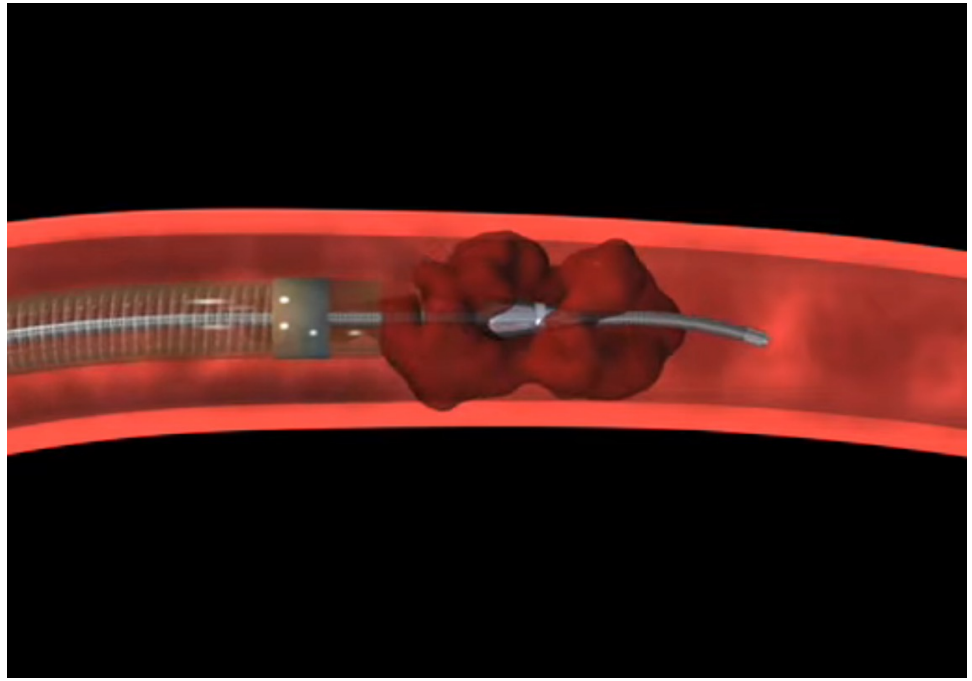
Dispositifs de thrombectomie

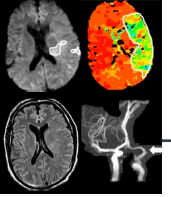
Stent retriever





Aspiration catheter





Thérapie combinée: « Règle des trois 6 »

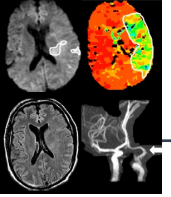
Règle des trois 6:

- NIHSS ≥ **6**
- ASPECTS ≥ **6**
- Thrombectomie initiée dans les **6**$^{\text{ères}}$ heures

American Heart Association | American Stroke Association
life is why

3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.

I



Thérapie combinée: Off Label

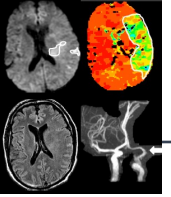
Off label:

- **NIHSS < 6**
- **ASPECT <6**

- **Site d'occlusion:**
  - M2? M3?
  - ACA ?
  - TB ?

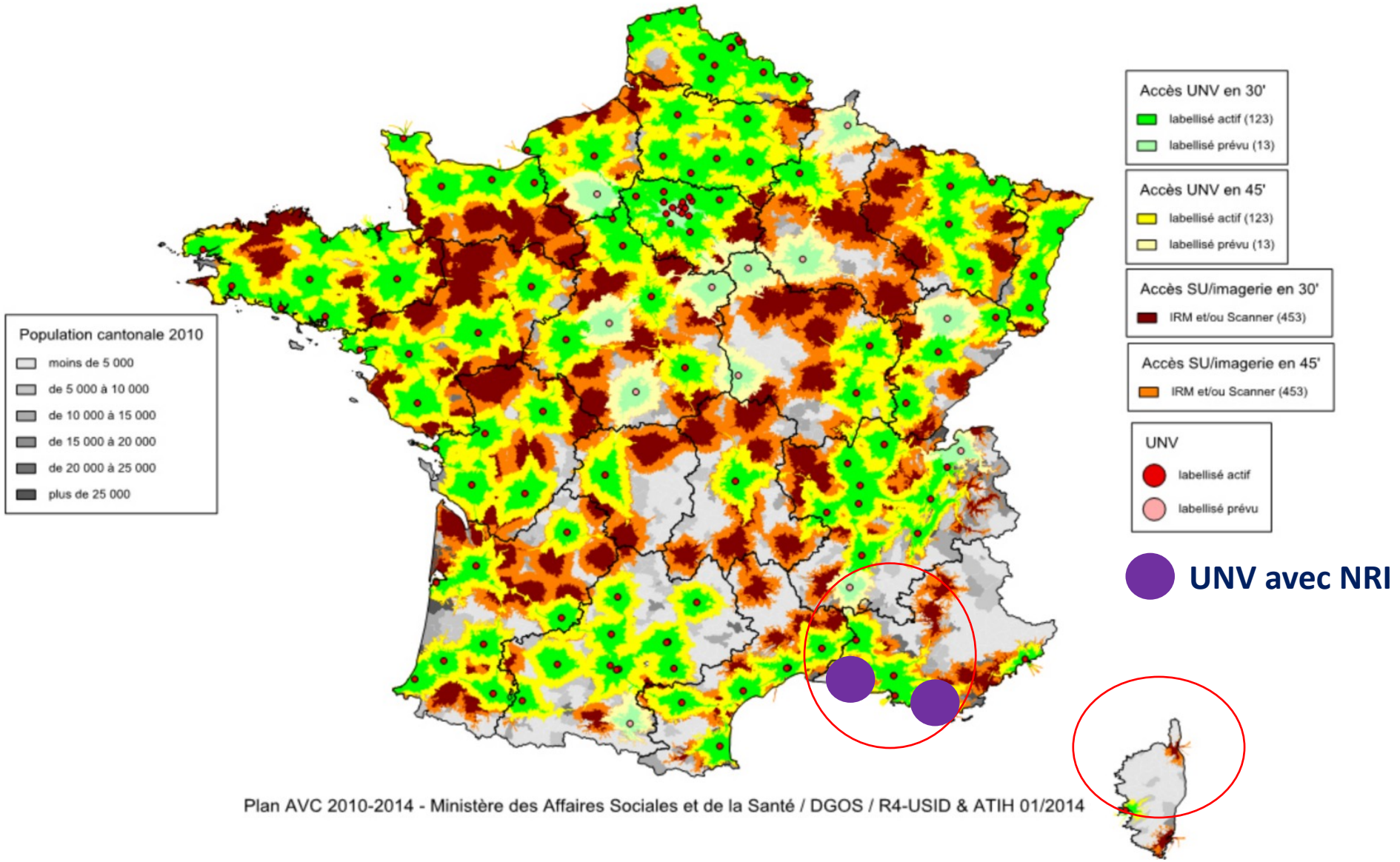
6. Although its benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have prestroke mRS score >1, ASPECTS <6, or NIHSS score <6, and causative occlusion of the internal carotid artery (ICA) or proximal MCA (M1). Additional randomized trial data are needed.	IIb

5. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the anterior cerebral arteries, vertebral arteries, basilar artery, or posterior cerebral arteries.	IIb
4. Although the benefits are uncertain, the use of mechanical thrombectomy with stent retrievers may be reasonable for carefully selected patients with AIS in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset and who have causative occlusion of the MCA segment 2 (M2) or MCA segment 3 (M3) portion of the MCAs.	IIb



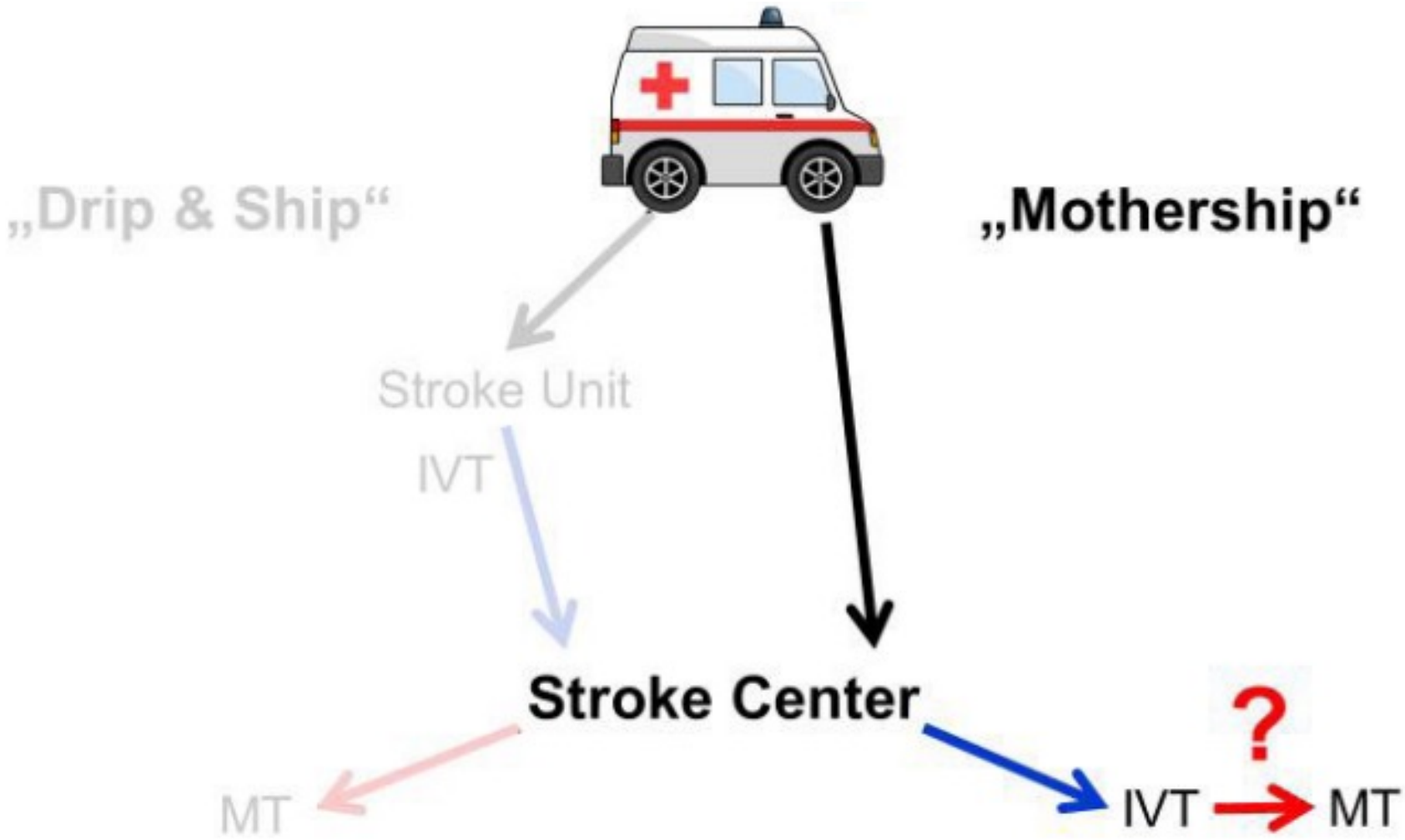
Phase aigue de l'infarctus cérébral: un défi organisationnel

Temps d'accès aux Unités NeuroVasculaires (UNV) actuelles et prévues
et aux Urgences avec plateau d'imagerie

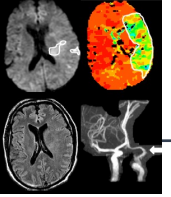


Plan AVC 2010-2014 - Ministère des Affaires Sociales et de la Santé / DGOS / R4-USID & ATIH 01/2014

Les modèles organisationnels: Mothership versus Drip and Ship ?



➔ **Aucun prédicteur pré-hospitalier de l’occlusion proximale validé**

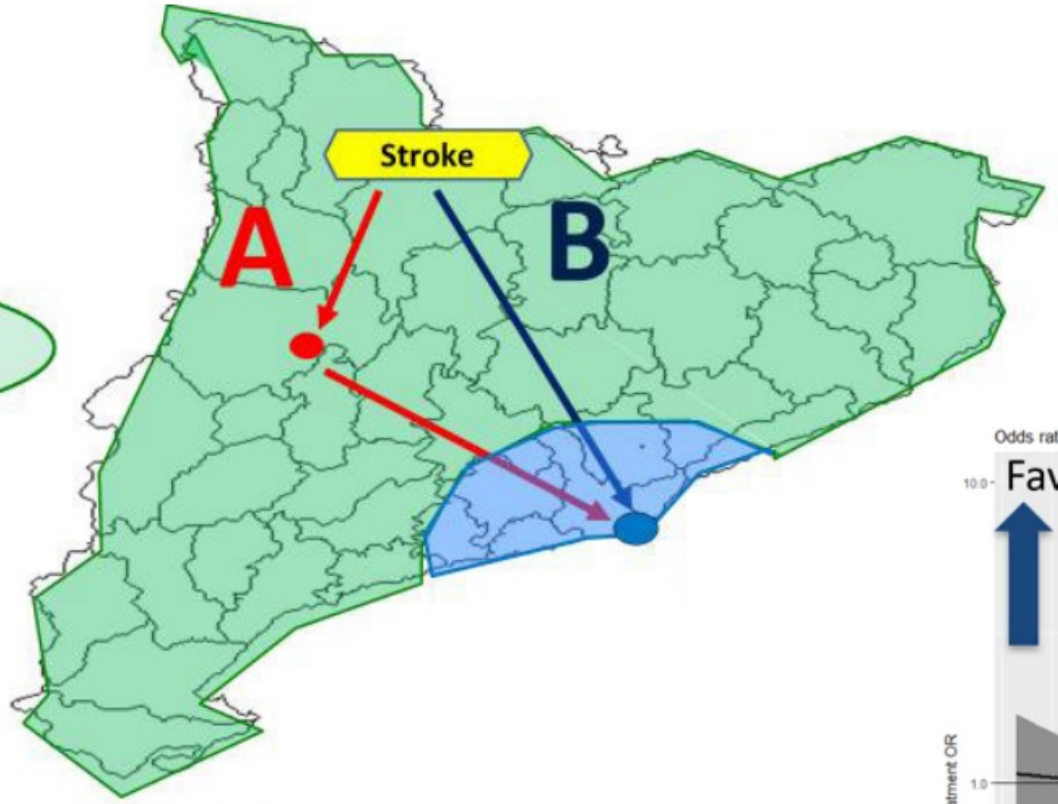


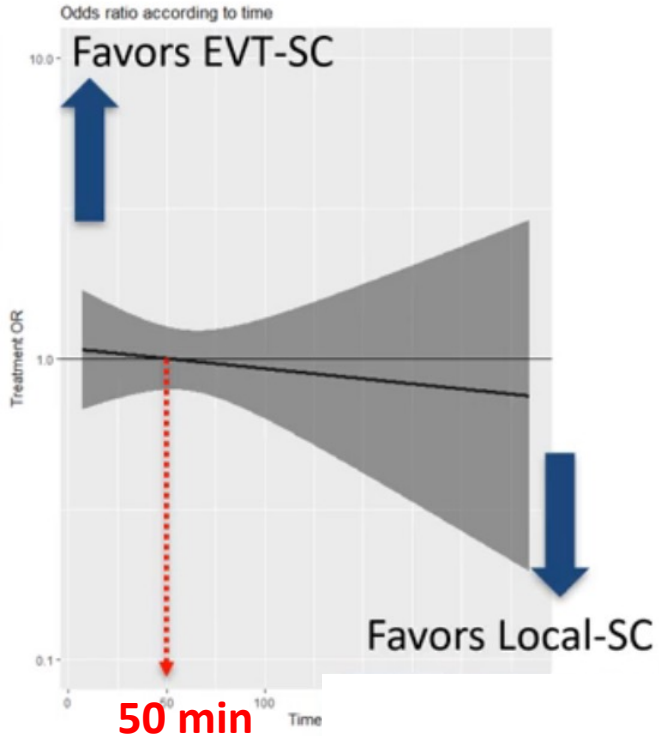
« Mothership » versus « Drip and Ship » : des essais randomisés

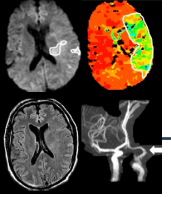
RACECAT

- ENDPOINTS:

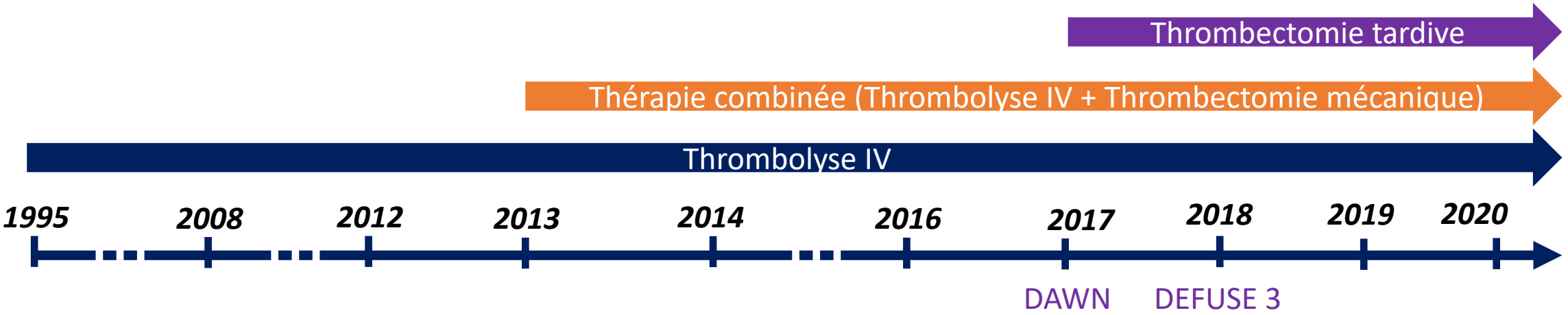
Option A Vs Option B ?

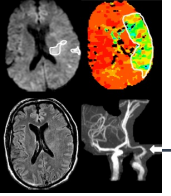






La thrombectomie tardive

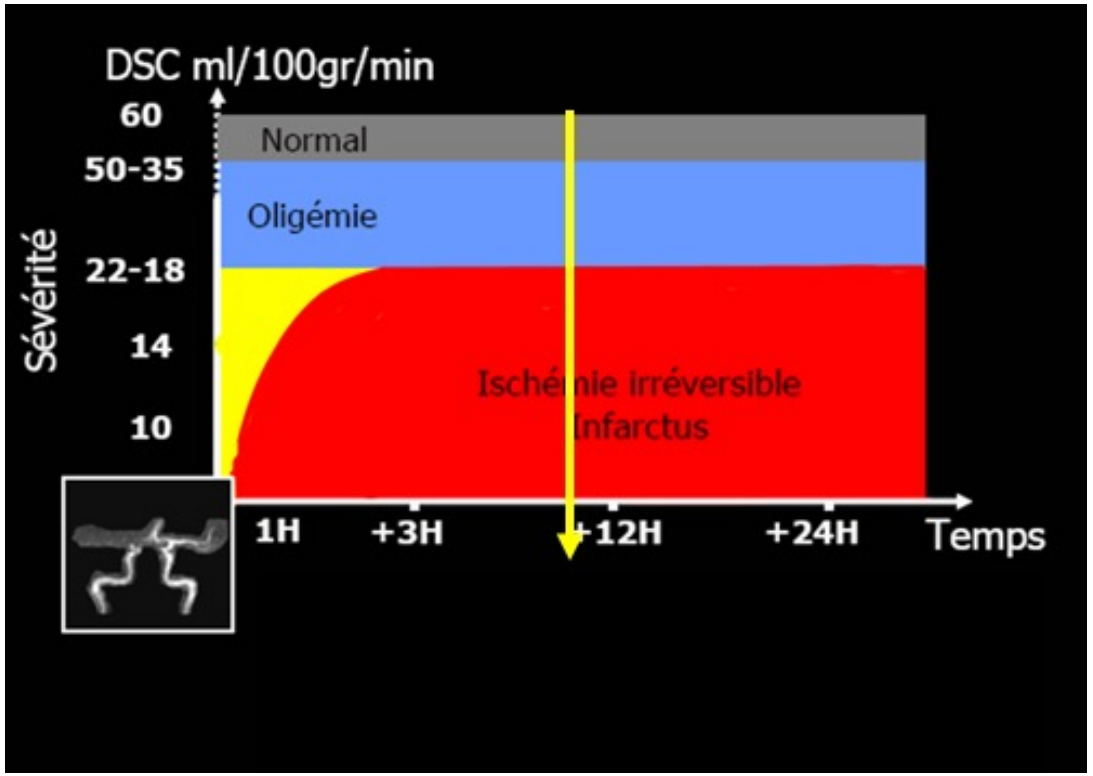




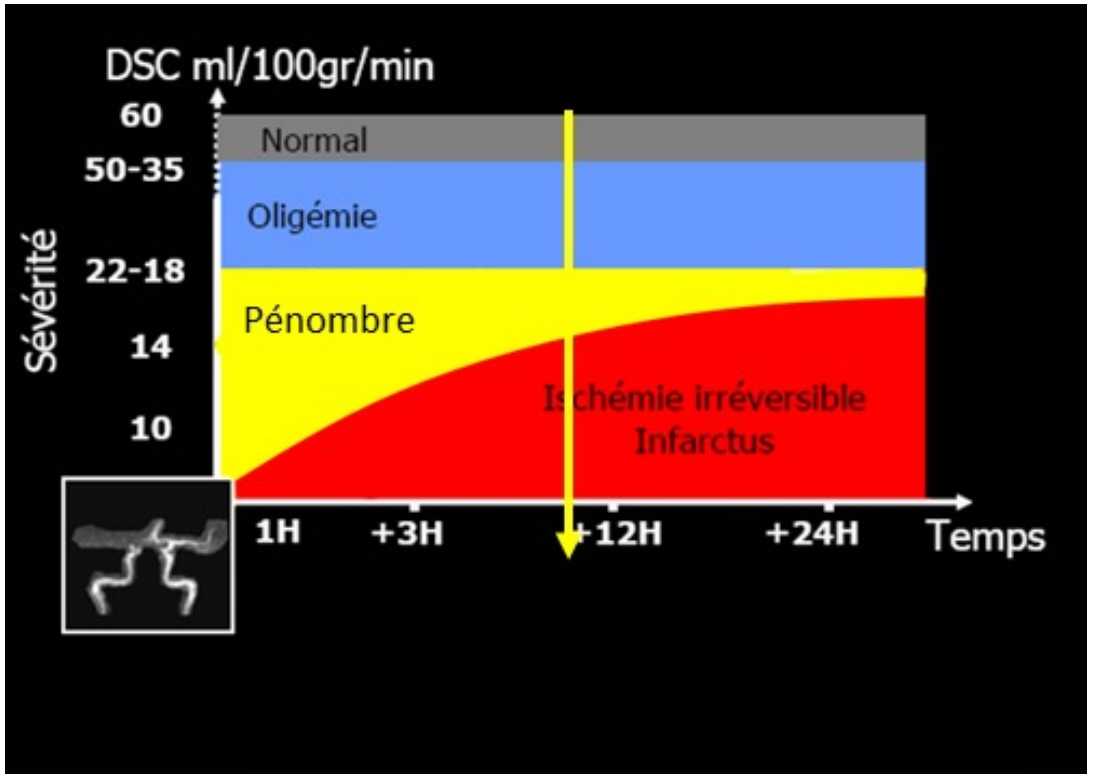
La thrombectomie tardive

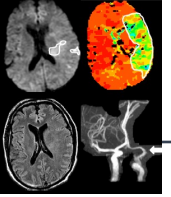
➔ **Existe-t-il encore de la pénombre ischémique au-delà de la 6ème heure ?**

Non



Oui





La thrombectomie tardive (Etudes DAWN et DEFUSE 3)

DAWN TRIAL

2017

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

defuse·3

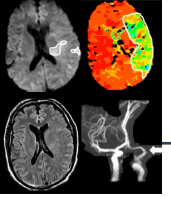
2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

G.W. Albers, M.P. Marks, S. Kemp, S. Christensen, J.P. Tsai, S. Ortega-Gutierrez, R.A. McTaggart, M.T. Torbey, M. Kim-Tenser, T. Leslie-Mazwi, A. Sarraj, S.E. Kasner, S.A. Ansari, S.D. Yeatts, S. Hamilton, M. Mlynash, J.J. Heit, G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*



Evaluation de la pénombre ischémique

AVCI associé à une occlusion de la CI intracrânienne et/ou du segment M1 de l'ACM

DAWN Vs. DEFUSE3 Key Inclusion and population Differences		
	DAWN	***DEFUSE-3***
enrollment NIHSS	>10	>=6
Age	>18	18-90
Infarct Size	Stratified, max 51ml	<70 ml
Imaging Inclusion	Mismatch between severity clinical deficit and infarct volume	Ischemia to penumbra ratio
Time inclusion (hrs post last seen normal)	6-24	6-16

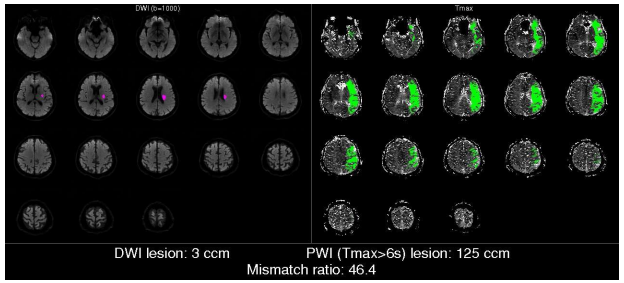
DAWN TRIAL

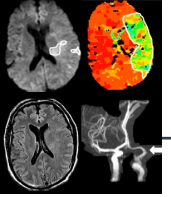
defuse·3

Mismatch clinico-radiologique:

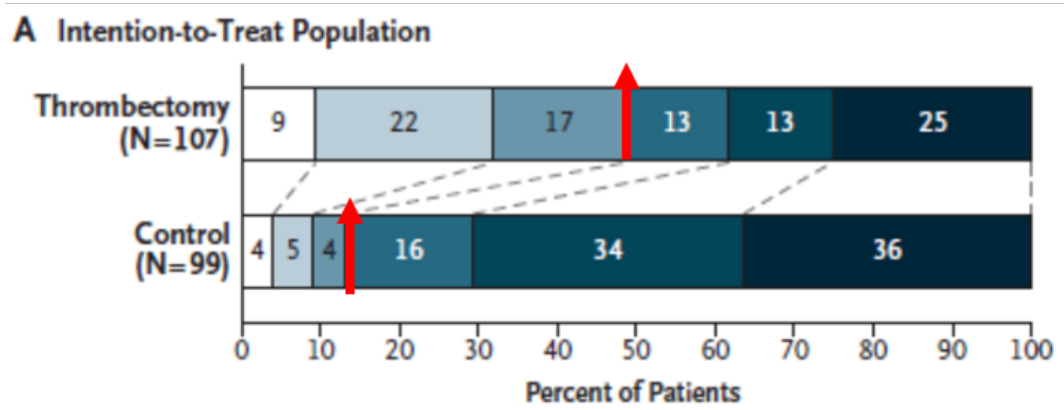
80 ans ou plus; NIHSS> ou égal à 10; DWI < 21 ml
< 80 ans; NIHSS > ou égale à 10; DWI < 31 ml
< 80 ans; NIHSS > 20 ou égal à 20; DWI entre 31 et 51 ml

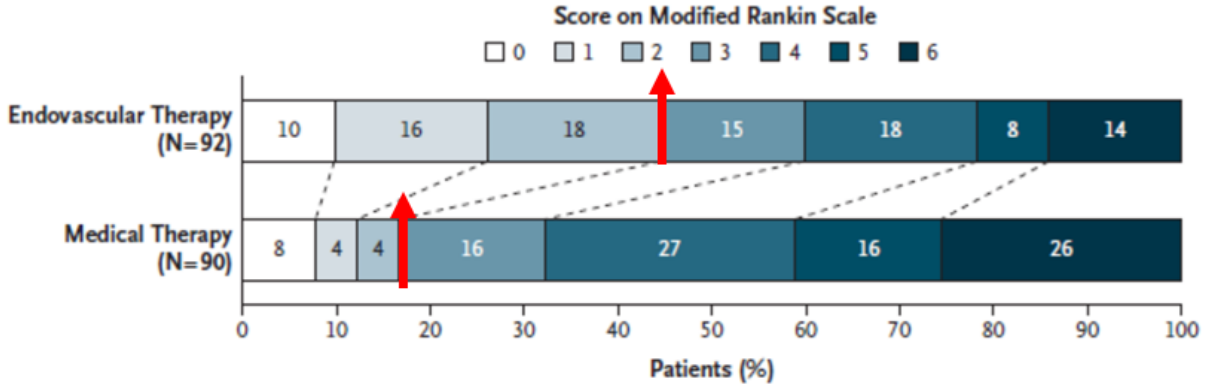
Mismatch radiologique:





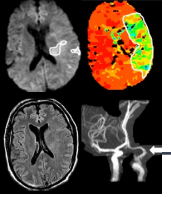
La thrombectomie tardive (Etudes DAWN et Defuse 3)





American Heart Association | American Stroke Association
life is why

7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	
8. In selected patients with AIS within 16 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.		IIa



La thrombectomie tardive…..Quelle organisation?

Mothership

versus

Drip and Ship

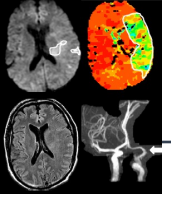
Eligibility for Endovascular Trial Enrollment in the 6- to 24-Hour Time Window

Analysis of a Single Comprehensive Stroke Center

Ashutosh P. Jadhav, MD, PhD; Shashvat M. Desai, MD; Cynthia L. Kenmuir, MD, PhD; Marcelo Rocha, MD, PhD; Matthew T. Starr, MD; Bradley J. Molyneaux, MD, PhD; Bradley A. Gross, MD; Brian T. Jankowitz, MD; Tudor G. Jovin, MD

Stroke

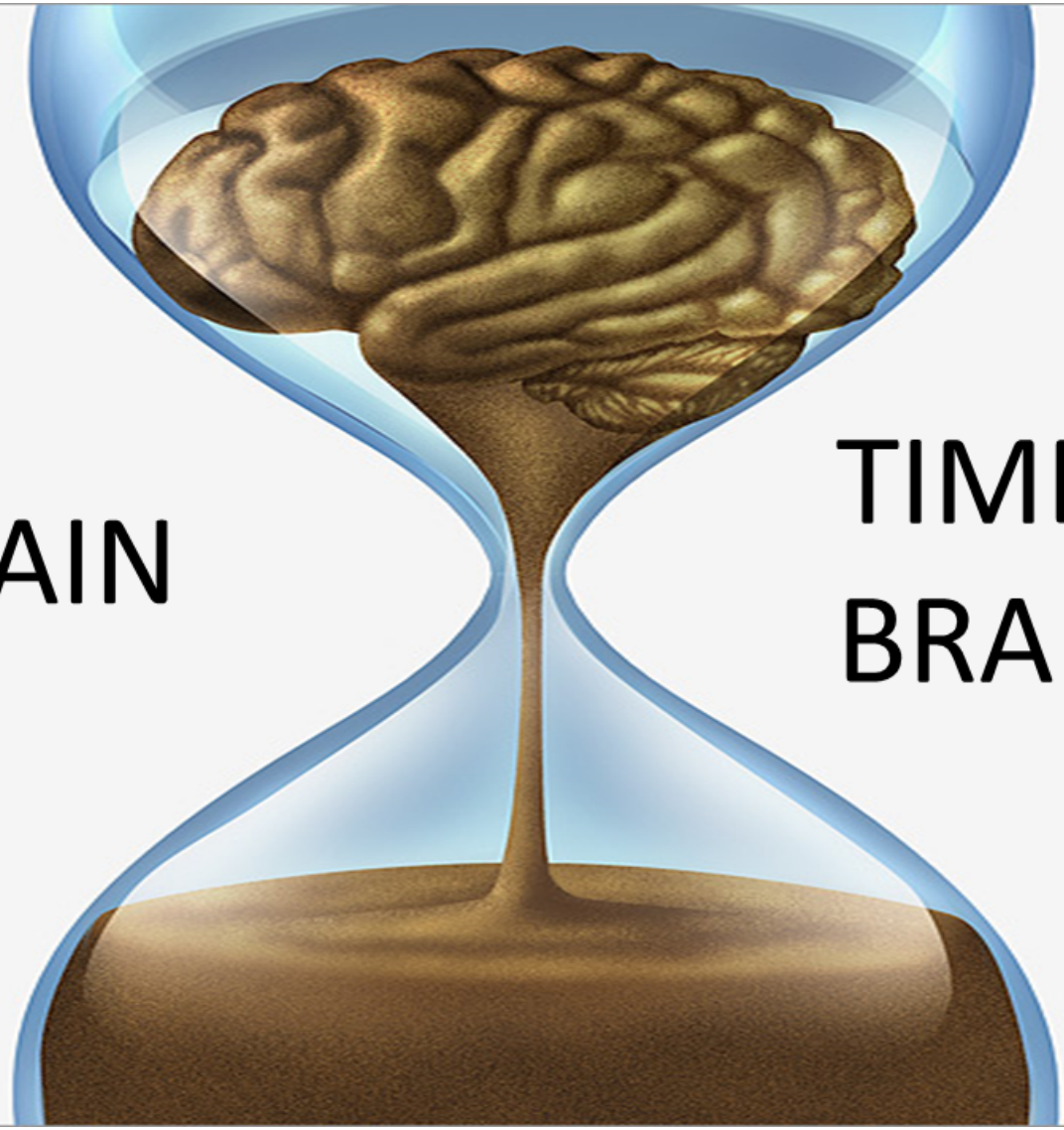
In summary, our analysis demonstrates that application of the DAWN and DEFUSE-3 enrollment criteria to an AIS population would impact 1.7% to 2.7% of total patients presenting to a comprehensive stroke center. These data have important implications for an anticipated rise in the number of thrombectomy-eligible patients and increased resource needs.



Take Home Message

- **La TM complète la thrombolyse IV dans les occlusions proximales de la circulation antérieure *(Imagerie vasculaire; Règle des 6)***
- **Pour les AVCI sans occlusion proximale, la thrombolyse IV reste le gold-standard (≤ 4h30)**
- **La thrombolyse IV peut être considérée pour les AVCi du réveil sur la base d'une sélection par IRM**
- **En cas d'occlusion proximale, la TM peut-être envisagée de 6 à 24 heures en fonction de l'évaluation de la pénombre ischémique**

TIME IS BRAIN



TIME LOST IS
BRAIN LOST