Hémorragie cérébrale : nouveaux modèles, nouveaux traitements
Session commune Société Française de Thrombose et d'Hémostase et Société Française Neuro-Vasculaire

Gestion de l'anticoagulation dans un contexte d'urgence : que disent les recommandations pour l'hémorragie cérébrale?

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Liens d'intérêt : Aguettant, Alexion, Bayer Healthcare, BMS-Pfizer, Boehringer Ingelheim, Sanofi, CSL Behring, LFB, Octapharma, Stago, Viatris

RECOMMANDATIONS FORMALISÉES D'EXPERTS

De la **Société Française de Médecine d'Urgence,**

la **Société Française d'Anesthésie-Réanimation et médecine péri-opératoire**

du Groupe d'intérêt en Hémostase Péri-opératoire

et **Société Française de Thrombose et d'Hémostase**

Gestion de l'anticoagulation dans un contexte d'urgence

2024

gihp.org

sfar.org

Anticoagulants et hémorragie intracérébrale

Spontaneous Intracerebral Hemorrhage

↗ anticoagulants over time

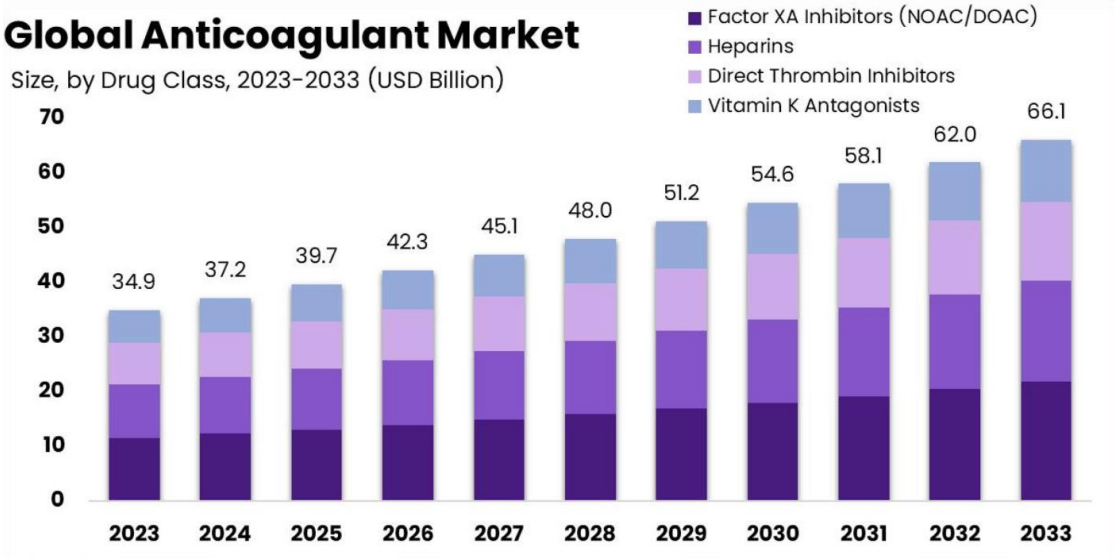
Béjot Y, Brain 2013

Anticoagulants : 8-27%

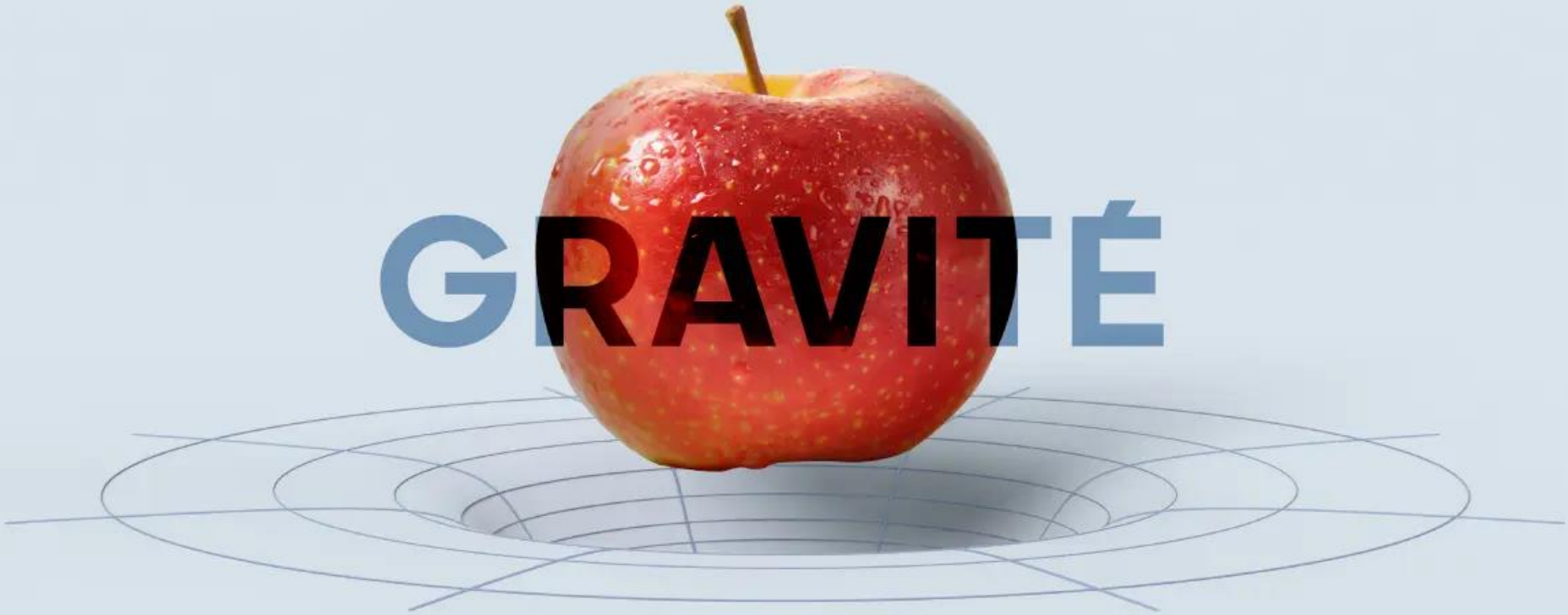
Larsen KT, J Am Heart Assoc. 2023

Ueno H. Sci Rep. 2024

Rodriguez-Luna DNeurology. 2024



https://market.us/report/anticoagulant-market/


GRAVITÉ

Meta-analysis of haematoma volume, haematoma expansion and mortality in intracerebral haemorrhage associated with oral anticoagulant use

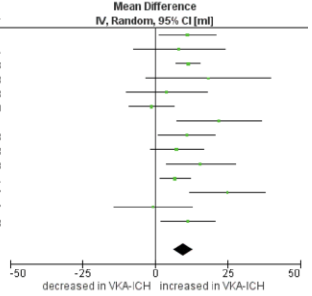
J Neurol 2019

Seiffge DJ, Goeldlin MB, Tatlisumak T, Lyrer P, Fischer U, Engelter ST, Werring DJ

Mean difference of ICH volume in VKA-ICH compared to non-OAC ICH

Study or Subgroup	VKA-ICH Mean [ml]	VKA-ICH SD [ml]	VKA-ICH Total	non OAC-ICH Mean [ml]	non OAC-ICH SD [ml]	non OAC-ICH Total	Weight	Mean Difference IV, Random, 95% CI [ml]	Year
Neau et al 2001	42	38.1	79	30.9	29.3	127	7.5%	11.10 [1.27, 20.93]	2001
Flibotte et al 2004	41.8	48.1	42	33.6	37.5	141	3.8%	8.20 [-7.61, 24.01]	2004
Flaherty et al 2008	23.5	15.2	51	12.1	4.4	207	15.2%	11.40 [7.19, 15.61]	2008
Cucchiara et al 2008	36	49.8	21	17.7	17.1	282	2.3%	18.30 [-3.09, 39.69]	2008
Fric-Shamji et al 2008	42	53.1	65	38	43.2	250	4.6%	4.00 [-9.98, 17.98]	2008
Toyoda et al 2009	23	31.1	67	24.3	34.2	738	9.7%	-1.30 [-9.14, 6.54]	2009
Yamashita et al 2011	43.1	69.9	94	21	26.1	295	4.4%	22.10 [7.66, 36.54]	2011
Ma et al 2013	29.8	39.8	69	18.9	24	335	7.6%	10.90 [1.16, 20.64]	2013
Horstmann et al 2013	25.7	30.9	51	18.3	23	155	8.1%	7.40 [-1.82, 16.62]	2013
Dequatre-Pontelle et al 2013	40.7	53.6	83	25	35	462	5.8%	15.70 [3.74, 27.66]	2013
Curtze et al 2014	19.9	29.8	132	13.1	16.6	878	13.5%	6.80 [1.60, 12.00]	2014
Roquer et al 2017	44.8	61.4	89	19.9	27.2	293	5.0%	24.90 [11.77, 38.03]	2017
Von der Brelie et al 2017	43.8	33.6	47	44.6	50.3	110	4.9%	-0.80 [-14.24, 12.64]	2017
Romem et al 2018	33.4	42.83	91	22.1	29.2	310	7.9%	11.30 [1.92, 20.68]	2018
Total (95% CI)			**981**			**4583**	**100.0%**	**9.66 [6.24, 13.07]**	

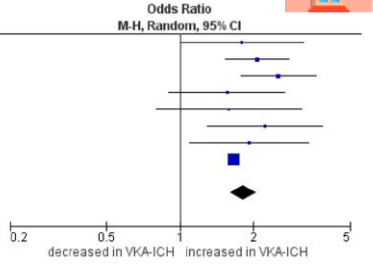
Heterogeneity: Tau² = 15.37; Chi² = 22.38, df = 13 (P = 0.05); I² = 42%
Test for overall effect: Z = 5.55 (P < 0.00001)



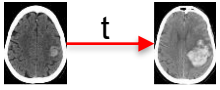
In-hospital mortality in VKA-ICH compared to non-OAC ICH

Study or Subgroup	VKA-ICH Events	VKA-ICH Total	non-OAC ICH Events	non-OAC ICH Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Neau et al 2001	35	79	39	127	4.2%	1.79 [1.00, 3.21]	2001
Foerch et al 2006	79	208	338	1483	12.9%	2.07 [1.53, 2.81]	2006
Flaherty et al 2006	63	190	139	851	10.2%	2.54 [1.79, 3.61]	2006
Fric-Shamji et al 2008	34	65	103	250	4.7%	1.57 [0.90, 2.71]	2008
Toyoda et al 2009	11	67	81	738	3.1%	1.59 [0.80, 3.16]	2009
Ma et al 2013	29	69	82	335	4.9%	2.24 [1.30, 3.83]	2013
Roquer et al 2017	24	89	47	293	4.5%	1.93 [1.10, 3.39]	2017
Inohara et al 2018	4903	15036	27297	121357	55.4%	1.67 [1.61, 1.73]	2018
Total (95% CI)		**15803**		**125434**	**100.0%**	**1.83 [1.61, 2.07]**	
Total events	5178		28126				

Heterogeneity: Tau² = 0.01; Chi² = 8.74, df = 7 (P = 0.27); I² = 20%
Test for overall effect: Z = 9.50 (P < 0.00001)

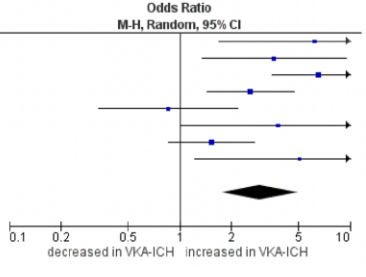


Rate of haematoma expansion (HE) in VKA-ICH compared to non-OAC ICH



Study or Subgroup	VKA-ICH Events	VKA-ICH Total	non-OAC ICH Events	non-OAC ICH Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Flibotte et al 2004	7	13	9	57	9.0%	6.22 [1.69, 22.88]	2004
Cucchiara et al 2008	10	18	69	267	12.1%	3.59 [1.36, 9.45]	2008
Fric-Shamji et al 2008	34	65	31	215	16.1%	6.51 [3.51, 12.08]	2008
Toyoda et al 2009	21	54	120	612	16.6%	2.61 [1.46, 4.67]	2009
Yamashita et al 2011	6	54	27	213	12.4%	0.86 [0.34, 2.20]	2011
Horstmann et al 2013	4	12	14	120	8.9%	3.79 [1.01, 14.22]	2013
Curtze et al 2014	21	63	94	383	16.7%	1.54 [0.87, 2.73]	2014
Von der Brelie et al 2017	5	23	4	77	8.2%	5.07 [1.23, 20.81]	2017
Total (95% CI)		**302**		**1944**	**100.0%**	**2.96 [1.76, 4.97]**	
Total events	108		368				

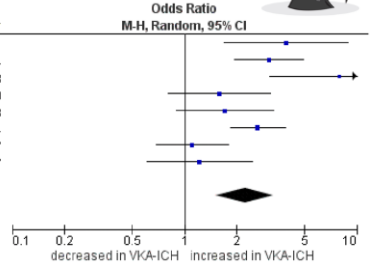
Heterogeneity: Tau² = 0.33; Chi² = 20.10, df = 7 (P = 0.005); I² = 65%
Test for overall effect: Z = 4.10 (P < 0.0001)



3-month mortality in VKA-ICH compared to non-OAC ICH

Study or Subgroup	VKA-ICH Events	VKA-ICH Total	non-OAC ICH Events	non-OAC ICH Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Radberg et al 1991	16	28	44	172	10.2%	3.88 [1.70, 8.83]	1991
Rosand et al 2004	53	102	86	333	14.8%	3.11 [1.96, 4.92]	2004
Cucchiara et al 2008	13	21	48	282	9.0%	7.92 [3.11, 20.16]	2008
Toyoda et al 2009	11	67	81	738	11.8%	1.59 [0.80, 3.16]	2009
Horstmann et al 2013	23	51	50	155	12.3%	1.73 [0.90, 3.29]	2013
Curtze et al 2014	67	132	242	868	15.9%	2.67 [1.84, 3.87]	2014
Roquer et al 2017	52	89	164	293	14.5%	1.11 [0.68, 1.79]	2017
Von der Brelie et al 2017	18	47	37	110	11.5%	1.22 [0.60, 2.49]	2017
Total (95% CI)		**537**		**2951**	**100.0%**	**2.24 [1.52, 3.31]**	
Total events	253		752				

Heterogeneity: Tau² = 0.21; Chi² = 24.17, df = 7 (P = 0.001); I² = 71%
Test for overall effect: Z = 4.06 (P < 0.0001)



AVK et mortalité

303 patients, imagerie à H6 et à H72

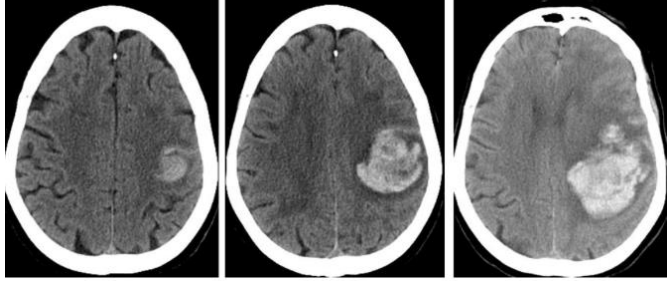
AVK : - volume initial de l'hématome + gros (30.6 versus 14.4 mL,*p*=0.03)
- expansion de l'hématome + fréquente (56% vs 26% p=0.006)
- mortalité + élevée (62% vs 17%, *p*=0.001)

Factors associated with mortality

	Odds Ratio	95% CI	*P*
Including baseline ICH volume and hemorrhage expansion in model			
Age, per year	1.07	1.03–1.10	<0.001
Male gender	2.02	0.86–4.74	0.11
OAT	1.97	0.54–7.16	0.30
Baseline ICH volume, per cc	1.05	1.03–1.07	<0.001
Hemorrhage expansion	4.03	1.87–8.70	<0.001

Cucchiara B. Stroke 2008

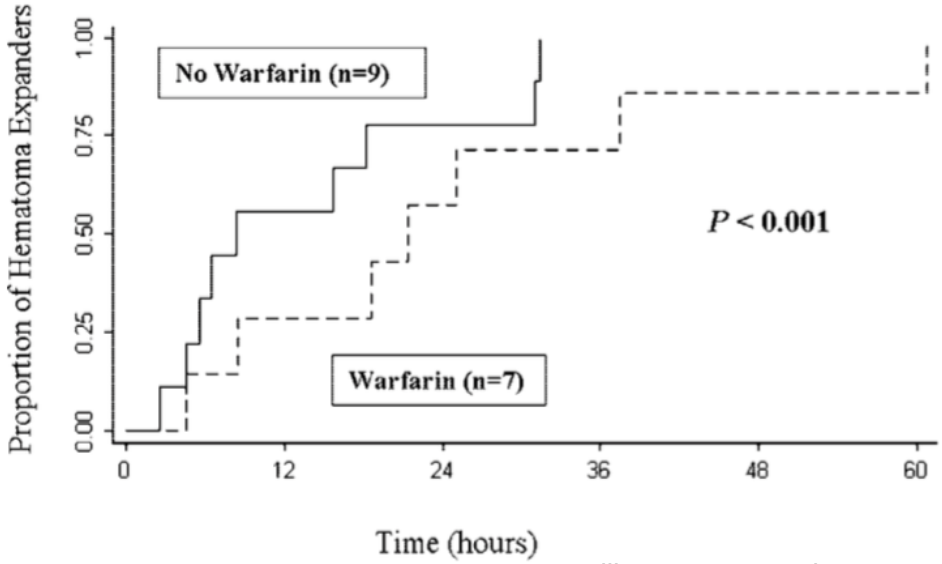
AVK et expansion de l'hématome



183 patients with intracerebral hemorrhage
23% (n=42) treated with warfarin

ICH expansion in patients with 2 or more CT scans

Characteristic	OR (95% CI)
Onset to baseline CT scan, h	0.99 (0.94–1.03)
Warfarin	6.22 (1.69–22.88)
Antiplatelet agent	0.42 (0.12–1.46)
Hypertension	0.31 (0.07–1.32)
ICH volume per 10 mL	0.84 (0.60–1.17)
IVH volume per 10 mL	1.12 (0.55–2.30)
Lobar location	1.02 (0.32–3.23)
GCS < 9	1.42 (0.25–8.16)
Glucose per 10 mg/dL	1.00 (0.81–1.22)
APOE ε4	0.46 (0.09–2.52)*
APOE ε2	5.13 (0.30–90.70)*

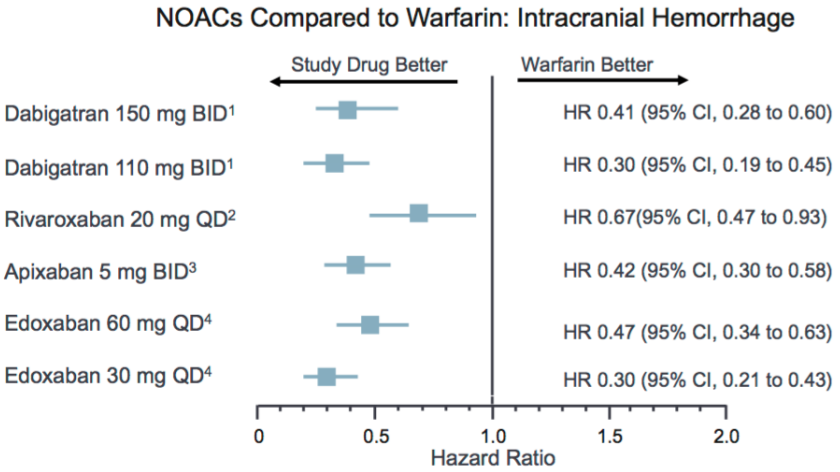


Flibotte JJ. Neurology 2004

Anticoagulants oraux directs

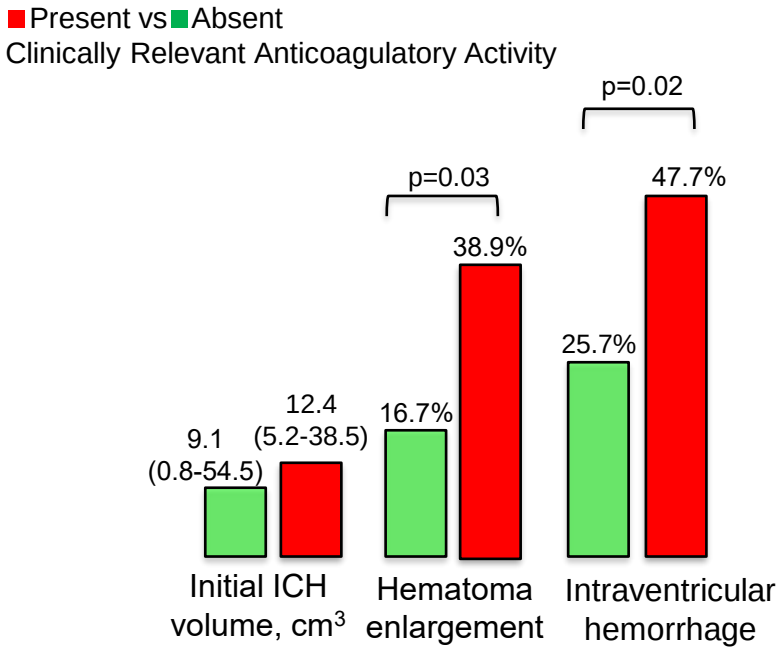
↘ Risque d'hémorragie intracrânienne vs AVK

4 essais dans la Fibrillation atriale



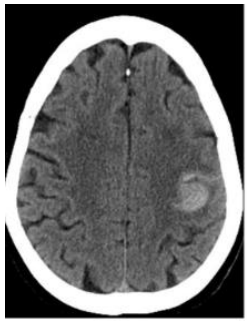
De Caterina R. Eur Heart J Supplements 2016

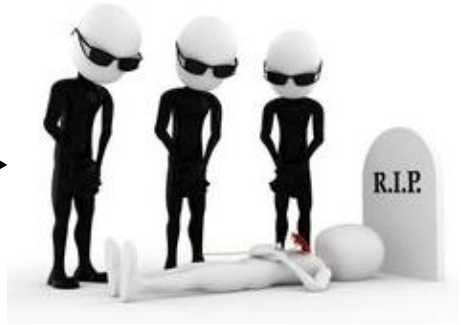
↗ Risque d'expansion de l'hématome



Gerner ST. Stroke 2019

Hémorragie cérébrale
associée aux anticoagulants

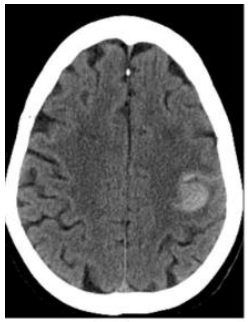




Réversion des anticoagulants

Effets secondaires ?
Risque thrombotique ?
Coûts ?

Hémorragie cérébrale
associée aux anticoagulants



Prévention
de l'expansion?

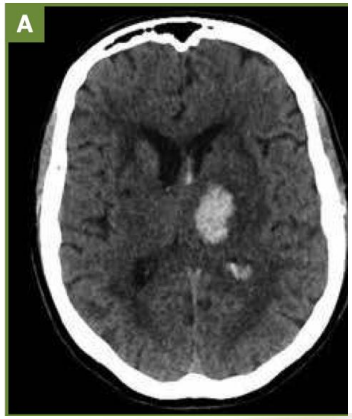
Amélioration
du pronostic ?

Anticoagulants et hémorragie intracérébrale

Anti-vitamine K

Dabigatran

Anti-Xa direct



Prend-elle un anticoagulant?
Si oui, quel anticoagulant?

RFE 2024 : Gestion de l'anticoagulation dans un contexte d'urgence

R1.1.1 – Chez un patient dont les informations relatives à la prise d'un traitement anticoagulant ne sont pas connues, les experts suggèrent que l'activité anti-Xa (HNF/HBPM) et le temps de thrombine (TT) soient évalués en plus de la mesure du TP/INR associé au TCA, pour exclure ou détecter la présence d'un anticoagulant en circulation.

AVIS D'EXPERTS (accord fort)

RFE 2024 : Gestion de l'anticoagulation dans un contexte d'urgence

R1.1.2 – Chez un patient dont le traitement anticoagulant est connu, les experts suggèrent de réaliser les tests suivants pour évaluer le niveau d'anticoagulation :

- AVK : INR ou examen de biologie médicale délocalisée (Point Of Care INR) ;
- HNF/HBPM/fondaparinux : activité anti-Xa avec calibration adaptée ;
- AOD : mesure de la concentration du médicament.

AVIS D'EXPERTS (accord fort)

R1.1.3 – Les experts suggèrent de ne pas utiliser les tests viscoélastométriques pour dépister et identifier un anticoagulant en circulation ou déterminer le niveau d'anticoagulation.

AVIS D'EXPERTS (accord fort)

RFE 2024 : Gestion de l'anticoagulation dans un contexte d'urgence

R2.1.2 – Chez un patient traité par anticoagulant et présentant une hémorragie intracrânienne ou un choc hémorragique, il est recommandé de réverser le traitement anticoagulant sans attendre le résultat des tests biologiques, sauf s'il est disponible en quelques minutes.

AVIS D'EXPERTS (accord fort)

Anti-vitamine K

Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial

Thorsten Steiner, Sven Poli*, Martin Griebe, Johannes Hüsing, Jacek Hajda, Anja Freiberger, Martin Bendszus, Julian Bösel, Hanne Christensen, Christian Dohmen, Michael Hennerici, Jennifer Kollmer, Henning Stetefeld, Katja E Wartenberg, Christian Weimar, Werner Hacke, Roland Veltkamp*

Lancet Neurol
2016

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	Fresh frozen plasma (n=23)	Prothrombin complex concentrate (n=27)	Treatment effect (95% CI)	p value
Primary outcome				
INR ≤1·2 within 3 h	2 (9%)	18 (67%)	OR 30·6 (4·7 to 197·9)*	0·0003
Secondary clinical outcomes				
Deaths at day 90	8 (35%)	5 (19%)	No proportional hazard assumed	0·14†
Secondary imaging outcomes				
Imaging data at 3 h¶				
Haematoma expansion (mL)	23·7 (28·4)	9·7 (20·9)	16·9 (2·5 to 31·3)‡	0·023
≥15% growth‖	16/22 (73%)**	15/26 (58%)**	OR 2·0 (0·6 to 7·3)*	0·29
≥33% growth‖	13/22 (59%)**	12 (44%)**	OR 3·8 (1·1 to 16·0)*	0·048
Imaging data at 24 h				
Haematoma expansion (mL)	22·1 (27·1)	8·3 (18·3)	16·4 (2·9 to 29·9)‡	0·018
≥15% growth or death‖	14/20 (70%)††	12/27 (44%)	OR 3·9 (1·0 to 17·6)*	0·044
≥33% growth or death‖	12/20 (60%) ††	8/27 (30%)	OR 4·8 (1·3 to 20·4)*	0·024

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Imaging data at 24 h				
Haematoma expansion (mL)	22·1 (27·1)	8·3 (18·3)	16·4 (2·9 to 29·9)‡	0·018
≥15% growth or death‖	14/20 (70%)††	12/27 (44%)	OR 3·9 (1·0 to 17·6)*	0·044
≥33% growth or death‖	12/20 (60%) ††	8/27 (30%)	OR 4·8 (1·3 to 20·4)*	0·024

Fresh frozen plasma versus prothrombin complex concentrate in patients with intracranial haemorrhage related to vitamin K antagonists (INCH): a randomised trial

Lancet Neurol
2016

Thorsten Steiner, Sven Poli*, Martin Griebe, Johannes Hüsing, Jacek Hajda, Anja Freiberger, Martin Bendszus, Julian Bösel, Hanne Christensen, Christian Dohmen, Michael Hennerici, Jennifer Kollmer, Henning Stetefeld, Katja E Wartenberg, Christian Weimar, Werner Hacke, Roland Veltkamp*

Mais arrêt précoce de l'essai

	Fresh frozen plasma (n=23)	Prothrombin complex concentrate (n=27)	Treatment effect (95% CI)	p value
Primary outcome				
INR ≤1·2 within 3 h	2 (9%)	18 (67%)	OR 30·6 (4·7 to 197·9)*	0·0003
Secondary clinical outcomes				
Deaths at day 90	8 (35%)	5 (19%)	No proportional hazard assumed	0·14†
Secondary imaging outcomes				
Imaging data at 3 h¶				
Haematoma expansion (mL)	23·7 (28·4)	9·7 (20·9)	16·9 (2·5 to 31·3)‡	0·023
≥15% growth‖	16/22 (73%)**	15/26 (58%)**	OR 2·0 (0·6 to 7·3)*	0·29
≥33% growth‖	13/22 (59%)**	12 (44%)**	OR 3·8 (1·1 to 16·0)*	0·048
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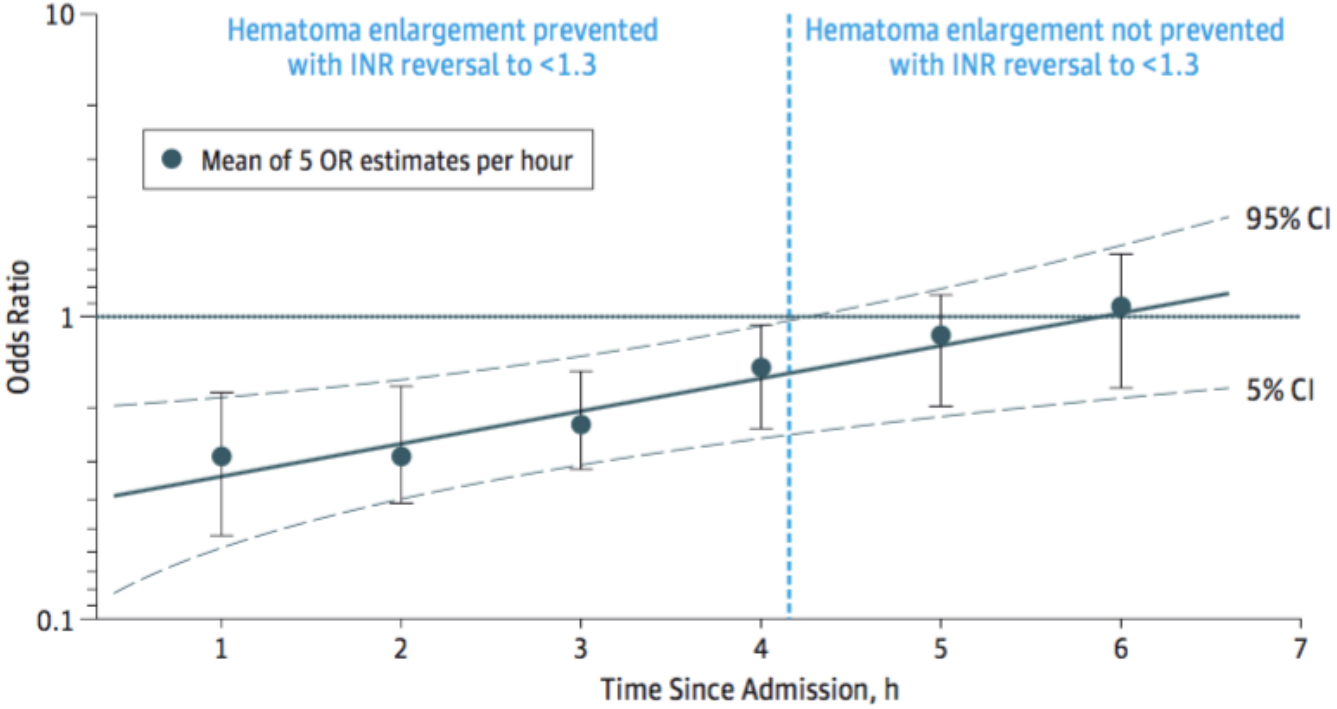
Délais d'antagonisation des AVK

Association of Timing and Extent of INR Reversal With Hematoma Enlargement



Kuramatsu JB. JAMA 2015

Time to Anticoagulation Reversal and Outcomes After Intracerebral Hemorrhage

JAMA Neurology
2024

Sheth KN, Solomon N, Alhanti B, Messe SR, Xian Y, Bhatt DL, Hemphill JC, Frontera JA, Chang RC, Danelich IM, Huang J, Schwamm L, Smith EE, Goldstein JN, Mac Grory B, Fonarow GC, Saver JL.

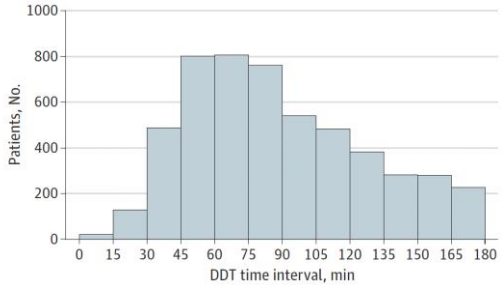
9492 patients with anticoagulation-associated ICH

↓

7469 (78.7%) received reversal therapy

4616 of 5429 (85.0%) taking warfarin
2856 of 4069 (70.2%) taking a DOAC

onset-to-treatment time: 232 (142-482) min
DTT time: 82 (58-117) min
DTT ≤60 min: n=1449 (27.7%)



Use of a **reversal agent** was associated with **reduced in-hospital mortality** in both unadjusted (OR 0.78; 95%CI, 0.70-0.87) and adjusted (adjOR 0.74; 95%CI 0.62-0.88) analyses.

DTT time ≤60 min associated with:

- decreased mortality and discharge to hospice (adj OR 0.82; 95%CI, 0.69-0.99)
- - no difference in functional outcome (mRS score)

Guideline-concordant administration of PCC and vitamin K is associated with decreased mortality in patients with severe bleeding under VKA treatment

Tazarourte K. Crit Care 2014

CRITICAL CARE 2014

EPAHK study

822 VKA-treated patients with severe hemorrhage

Type of hemorrhage	All patients (*N* = 822)	Alive (*N* = 712)	Dead (*N* = 110)	*P*
Intracranial	262 (32%)	176 (25%)	86 (78%)	<0.001
Gastrointestinal	264 (32%)	253 (36%)	11 (10%)	<0.001
Deep-muscle hematomas	107 (13%)	103 (15%)	4 (4%)	<0.001
"Other"***	189 (23%)	180 (25%)	9 (8%)	<0.001
Admission INR	4.7 ± 3.4	4.7 ± 3.5	4.4 ± 2.7	0.236
Normal (≤1.5)	45 (5%)	40 (6%)	5 (5%)	0.385
Therapeutic (>1.5 to 4)	394 (48%)	341 (48%)	53 (48%)	
Supratherapeutic (>4)	345 (42%)	300 (42%)	45 (41%)	
VKA reversal				
Guideline-concordant	313 (38%)	280 (39%)	33 (30%)	

Guideline-concordant VKA reversal?

≥ 20 IU/kg FIX equivalent PCC

≥ 5 mg of vitamin K

< 8 hours after admission

Guideline-concordant administration of PCC and vitamin K is associated with decreased mortality in patients with severe bleeding under VKA treatment

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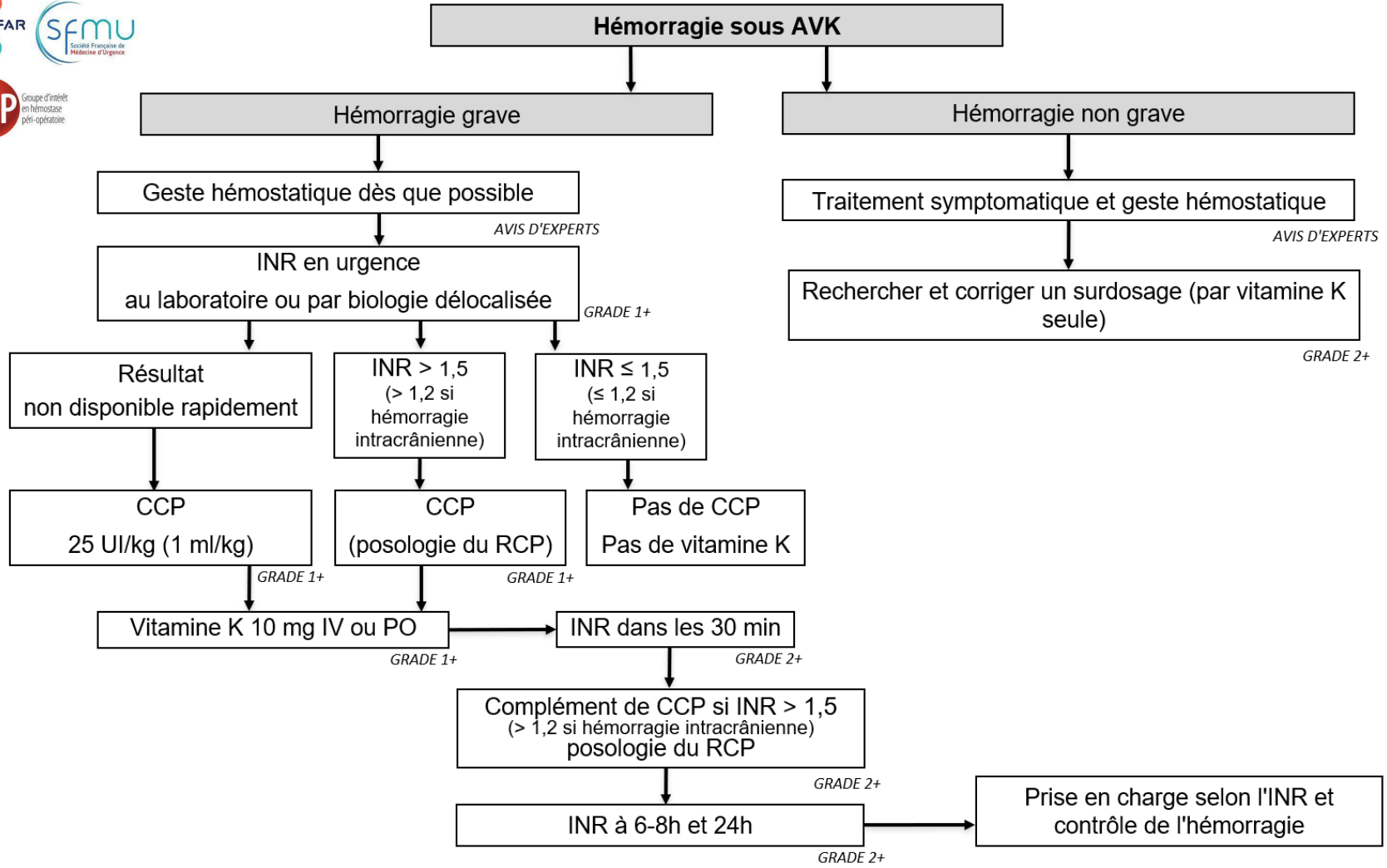
≥ 5 mg of vitamin K
< 8 hours after admission

Seven-day mortality
Multivariate analysis
Guideline-concordant VKA reversal
OR = 2.15 (1.20 to 3.88); p= 0.011

Mortality reduction also observed when only ICH was considered
OR = 3.23 (1.53 to 6.79); p=0.002

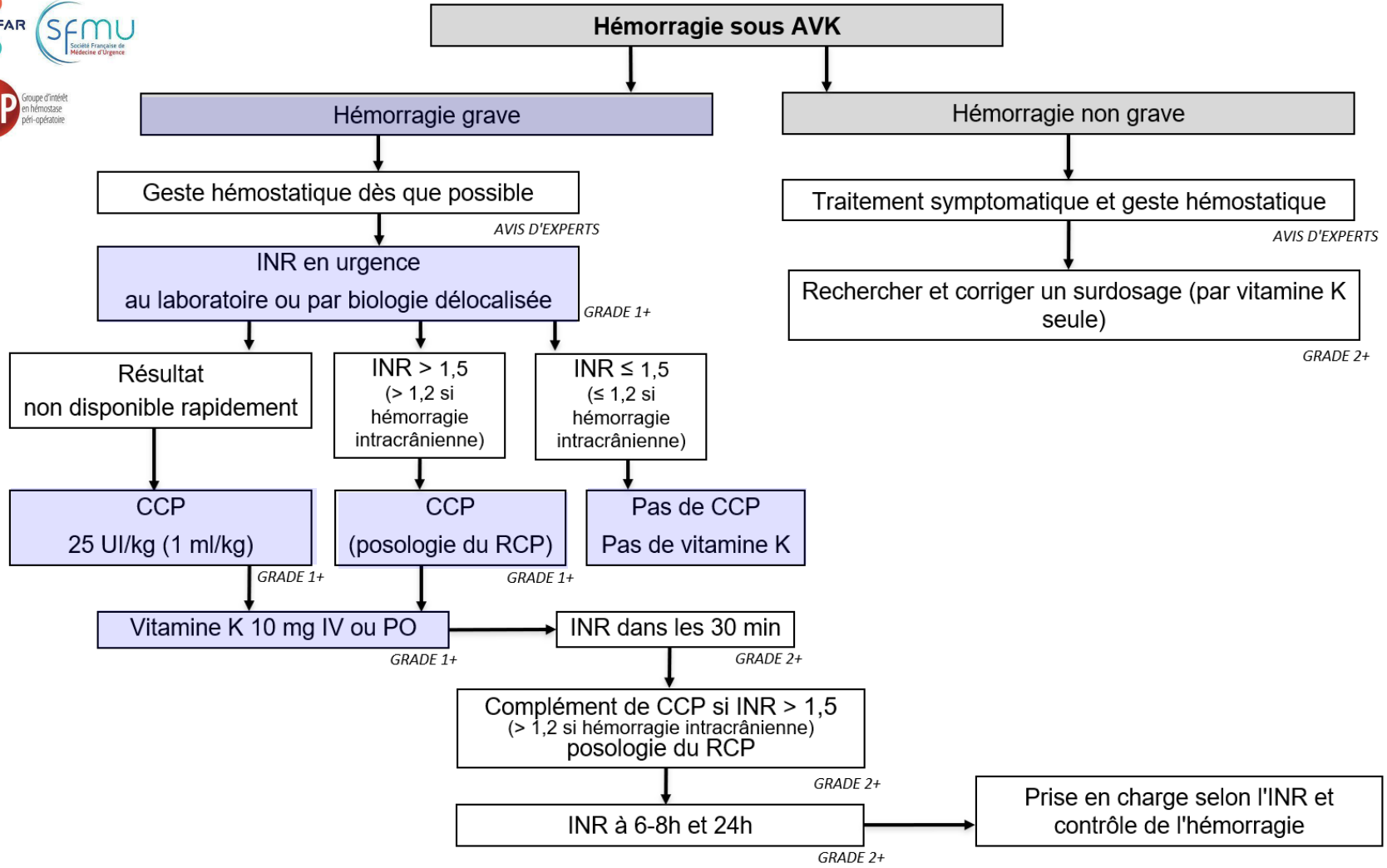
RFE 2024

SFAR · SFMU Société Française de Médecine d'Urgence · SFTH Société Française de Thrombose et d'Hémostase · GIHP Groupe d'Intérêt en Hémostase Péri-opératoire



RFE 2024

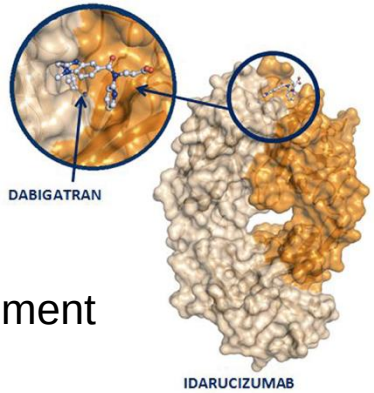
SFAR SFMU SFTH GIHP



Anticoagulants oraux directs

Idarucizumab for Dabigatran Reversal

humanized monoclonal antibody fragment



Idarucizumab for Dabigatran Reversal
Full Cohort Analysis

Charles V. Pollack, Jr., M.D., Paul A. Reilly, Ph.D., Joanne van Ryn, Ph.D.,

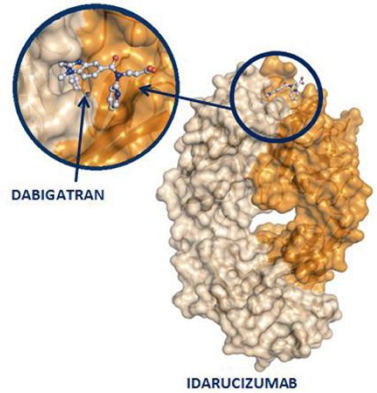
RE-VERSE AD™

2017

503 Dabigatran treated patients

- Uncontrolled bleeding
- Urgent procedure

→ 5 g idarucizumab IV → Diluted thrombin time [unbound dabigatran]



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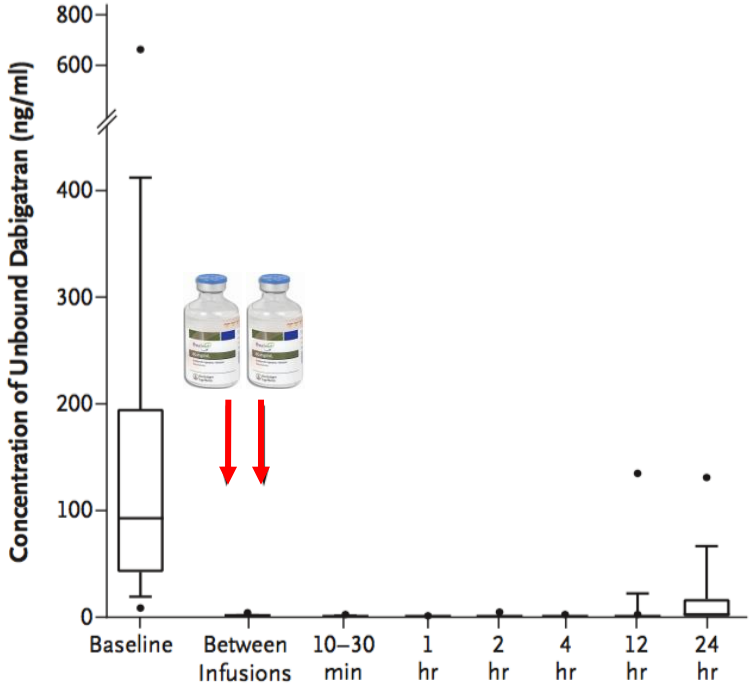

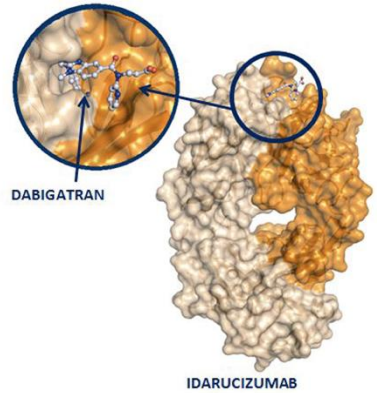

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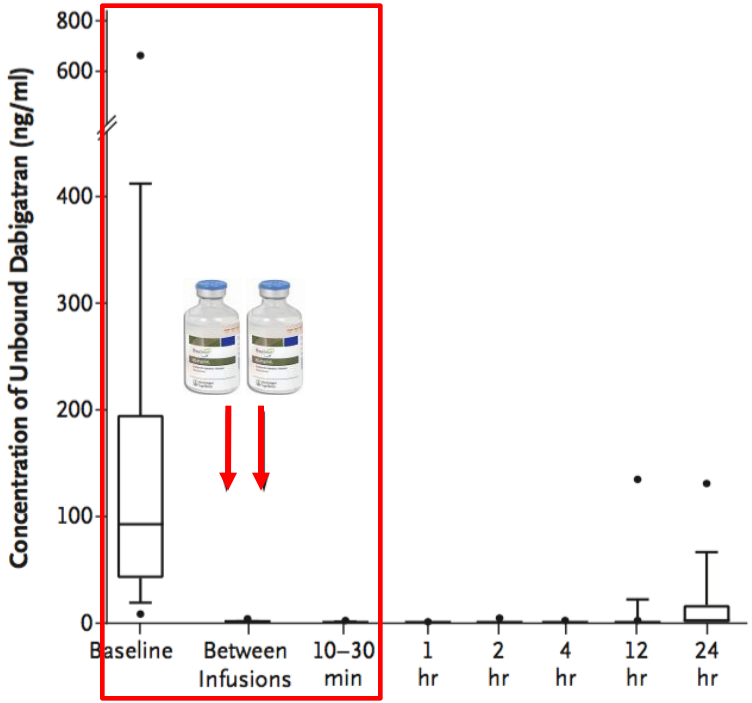

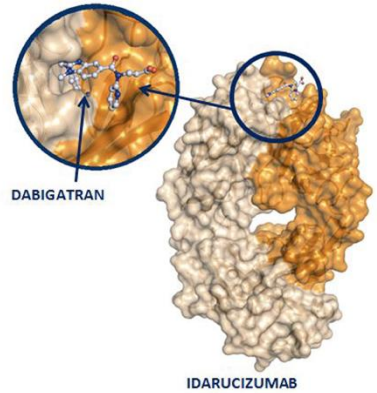

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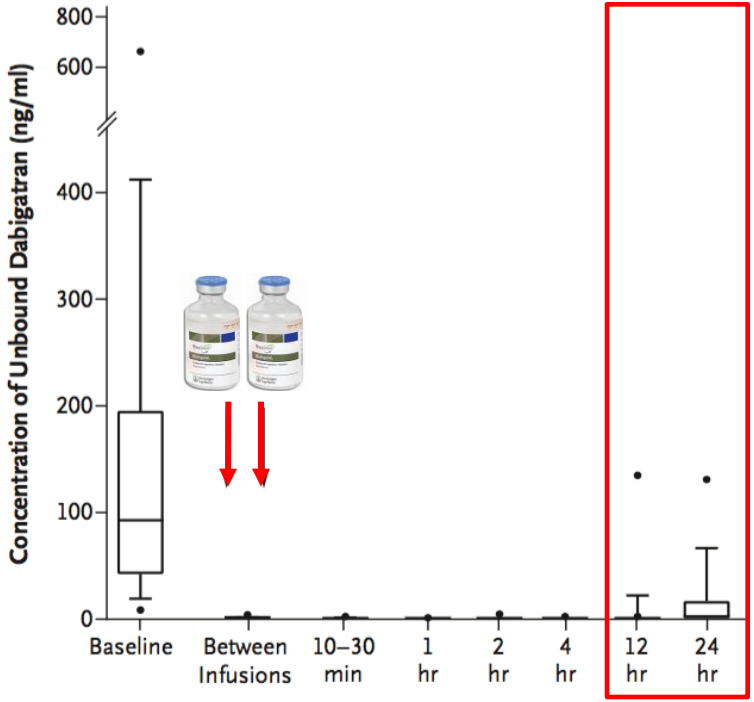
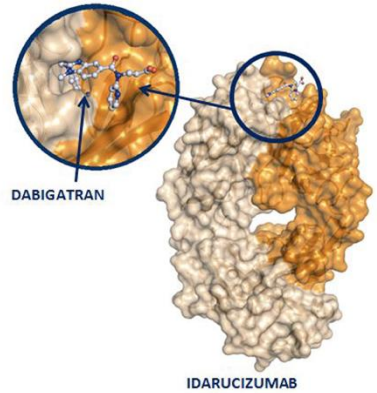


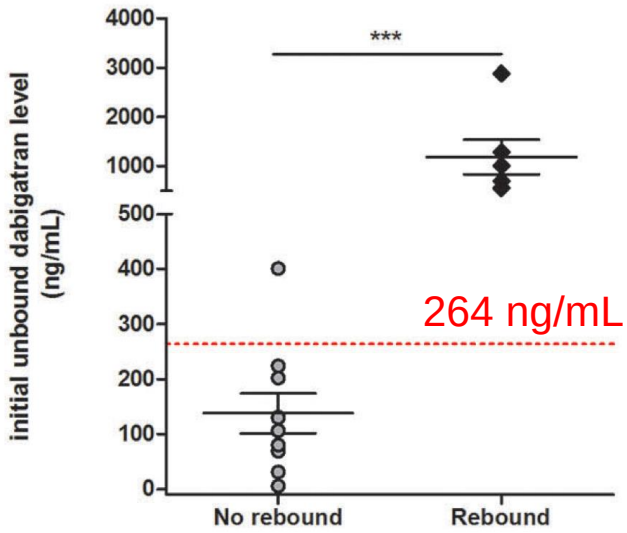


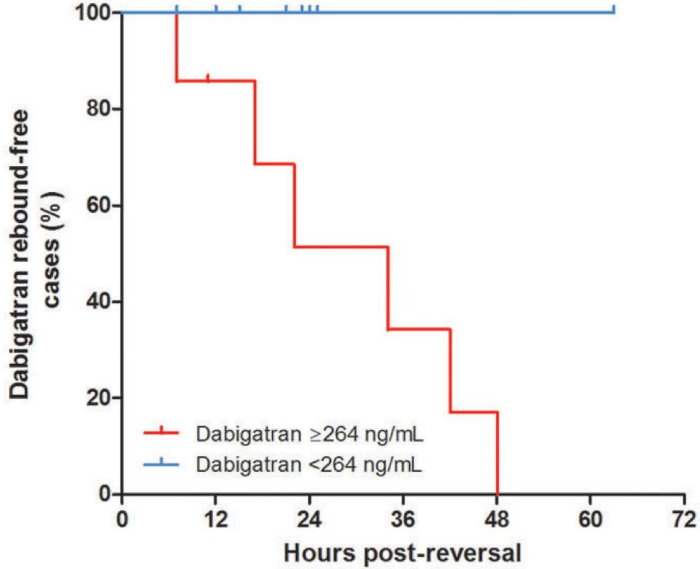
- Re increase [dabigatran](23%)
- Recurrent bleeding
- Discuss 2nd administration

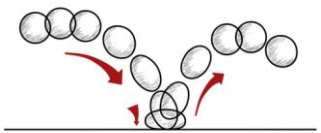
Dabigatran Level Before Reversal Can Predict Hemostatic Effectiveness of Idarucizumab in a Real-World Setting

frontiers in Medicine 2020

Gendron N, Chocron R, Billoir P, Brunier J, Camoin-Jau L, Tuffigo M, Faille D, Teissandier D, Gay J, de Raucourt E, Suner L, Bonnet C, Martin AC, Lasne D, Ladhari C, Lebreton A, Bertoletti L, Ajzenberg N, Gaussem P, Morange PE, Le Cam Duchez V, Viallon A, Roy PM, Lillo-le Louët A, Smadja DM.







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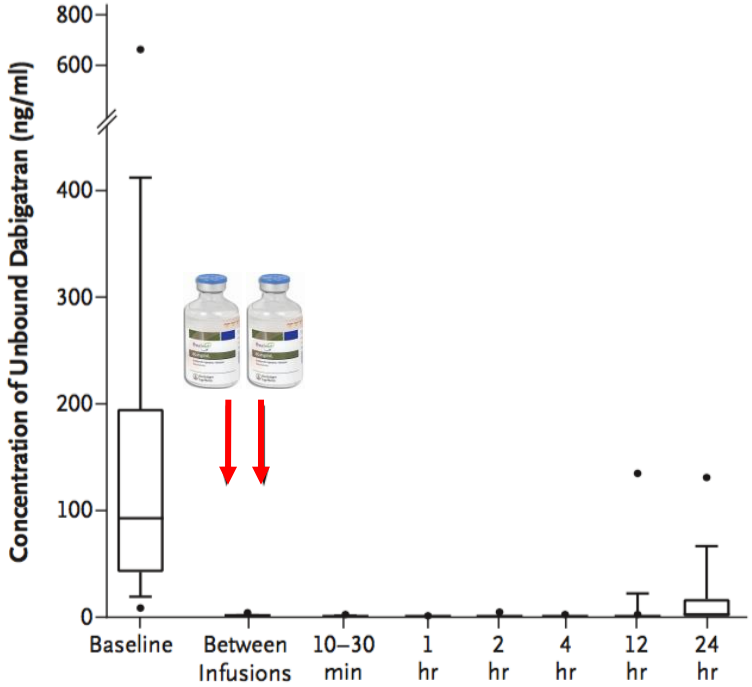
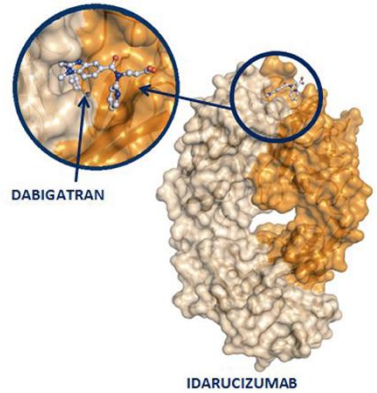




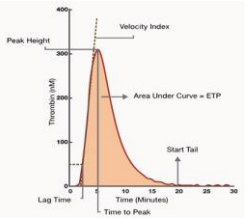
Thromboembolic events

4.8% within 30 days after idarucizumab administration

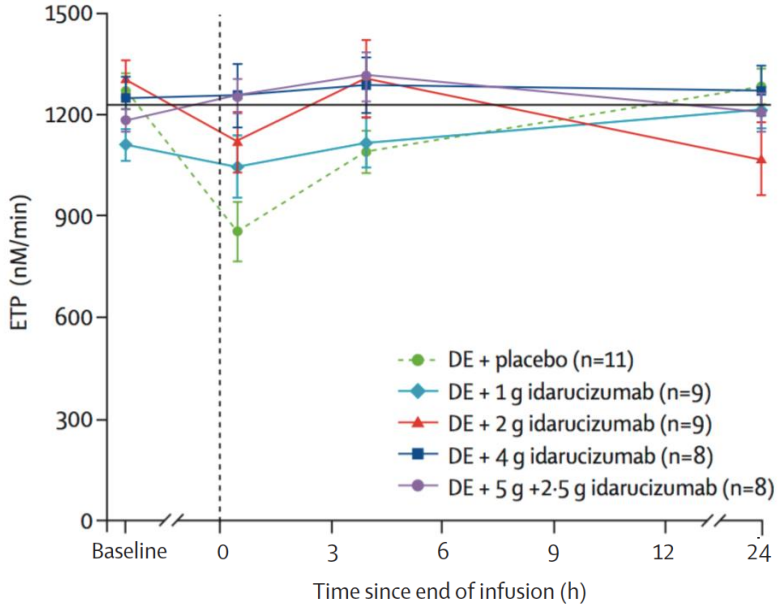
Safety, tolerability, and efficacy of idarucizumab for the reversal of the anticoagulant effect of dabigatran in healthy male volunteers: a randomised, placebo-controlled, double-blind phase 1 trial

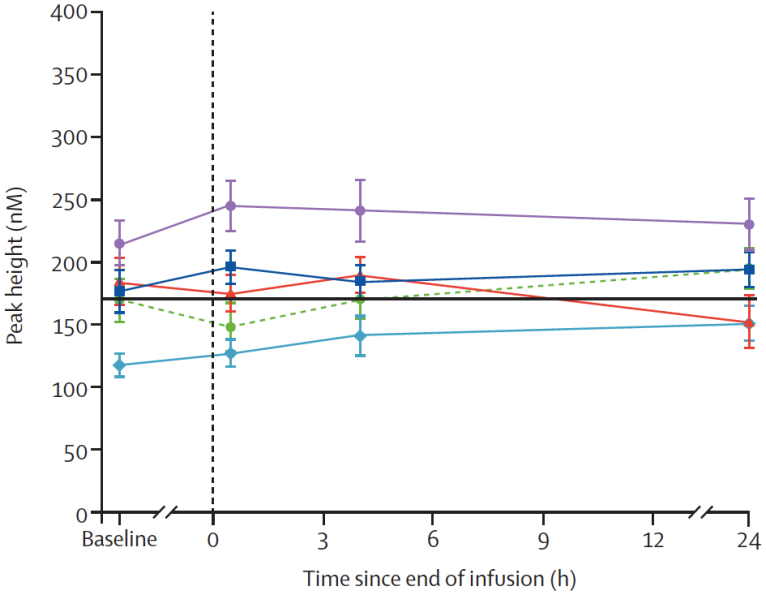
Stephan Glund, Joachim Stangier, Michael Schmohl, Dietmar Gansser, Stephen Norris, Joanne van Ryn, Benjamin Lang, Steven Ramael, Viktoria Moschetti, Fredrik Gruenenfelder, Paul Reilly, Jörg Kreuzer

THE LANCET 2015



Génération de thrombine chez des volontaires sains prenant du dabigatran (220 mg x2/j 3j) puis de l'idarucizumab





RFE 2024

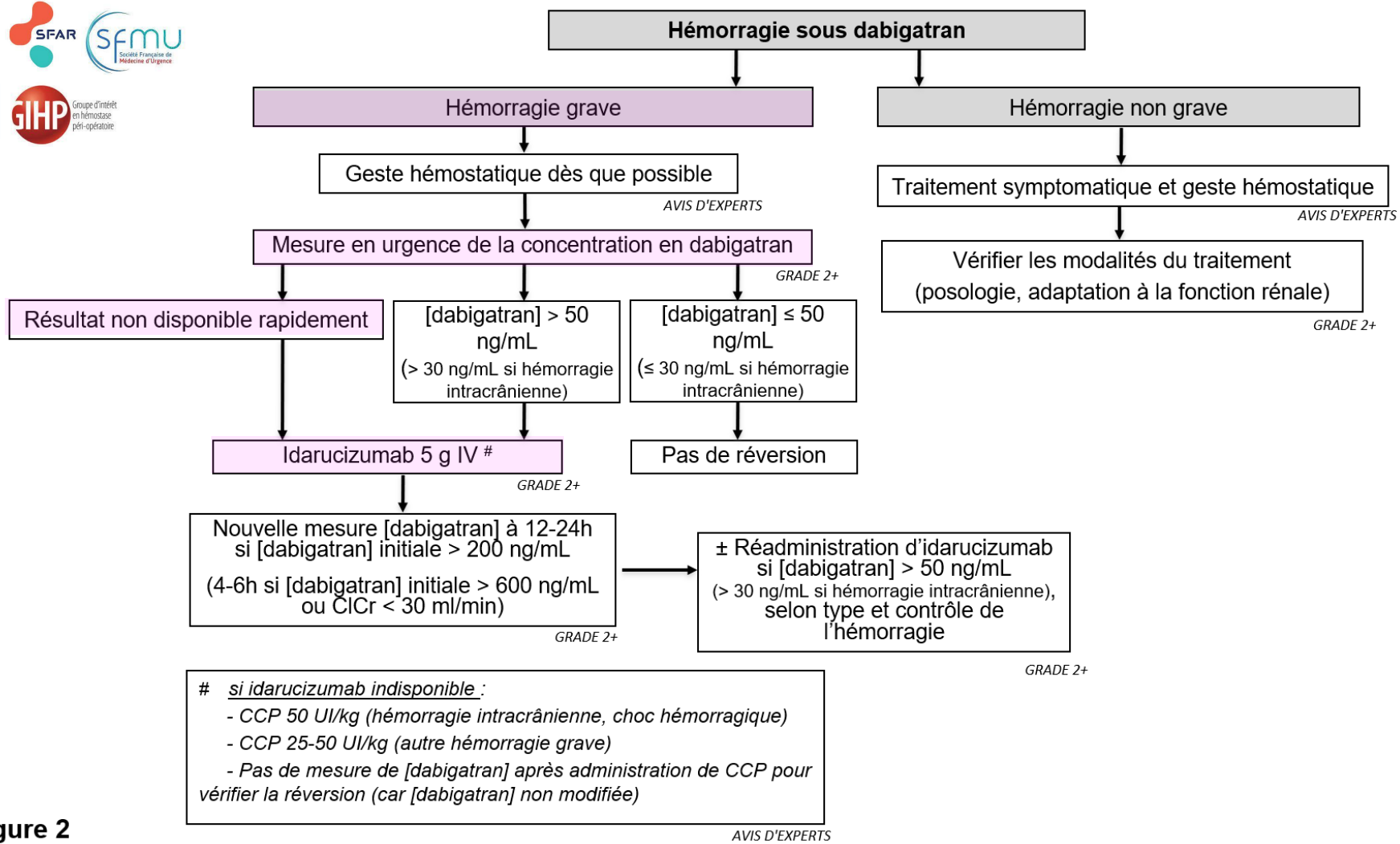


Figure 2

RFE 2024

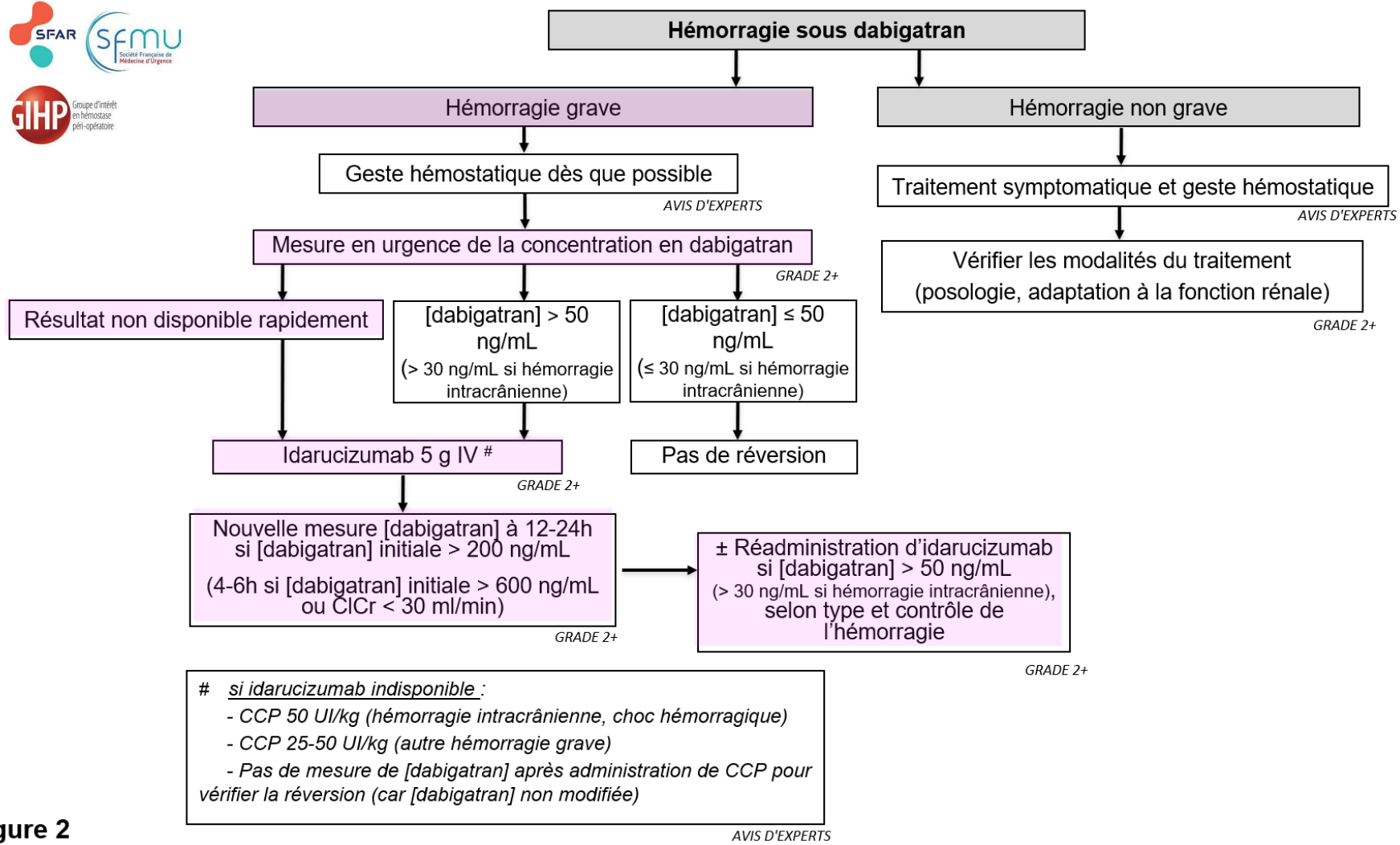
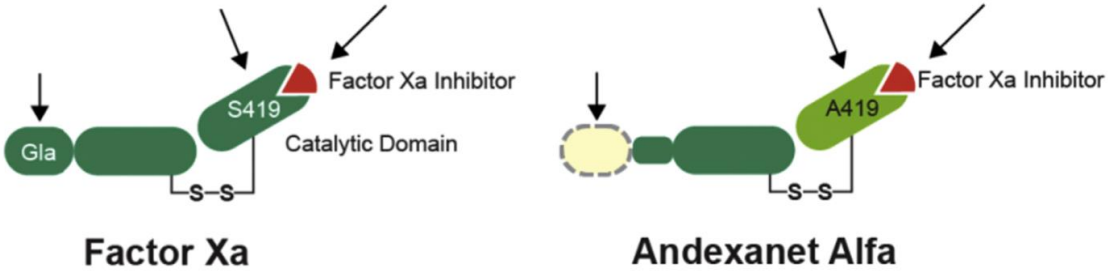


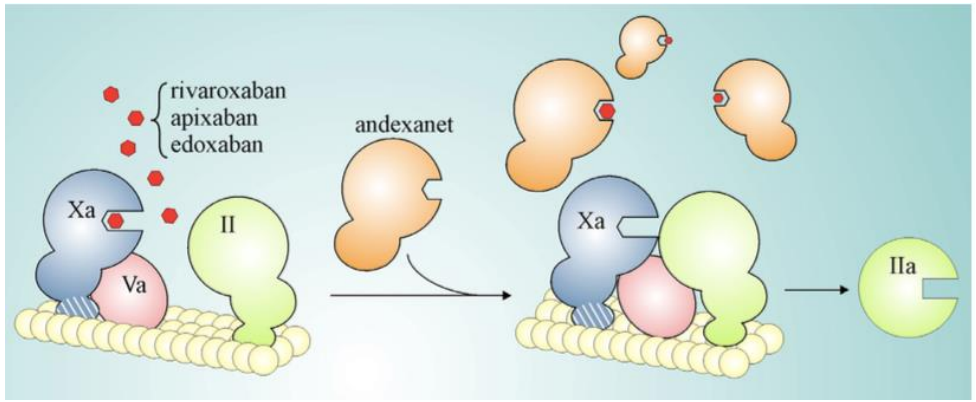
Figure 2

Anticoagulants anti-Xa direct

Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity

Recombinant human FXa variant





Milling TJ. Am J Med. 2016

Fredenburgh JC, Weitz JI. Circulation Research 2016

Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors

ANNEXA-4 Investigators
February 7 2019

Hémorragies majeures sous anti-Xa → Andexanet bolus + IVSE sur 2h

n=352

128 rivaroxaban
194 apixaban
20 enoxaparin
10 edoxaban

riva<7h edox enox	*800 mg IVL + 960 mg IVSE*
riva>7h apix	*400 mg IVL + 480 mg IVSE*

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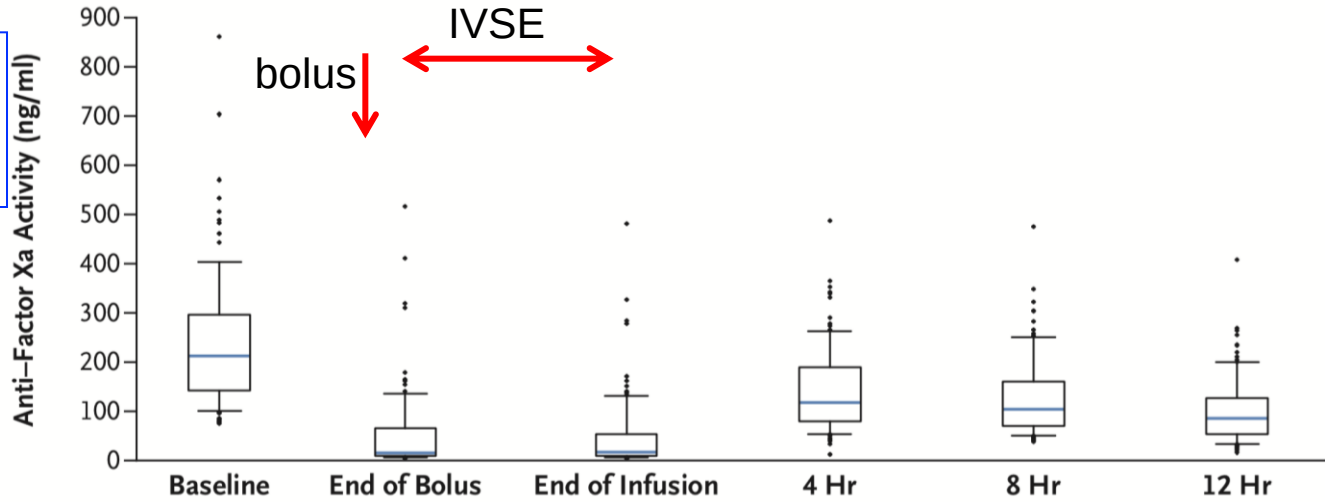
Rivaroxaban
>75 ng/mL
n=100



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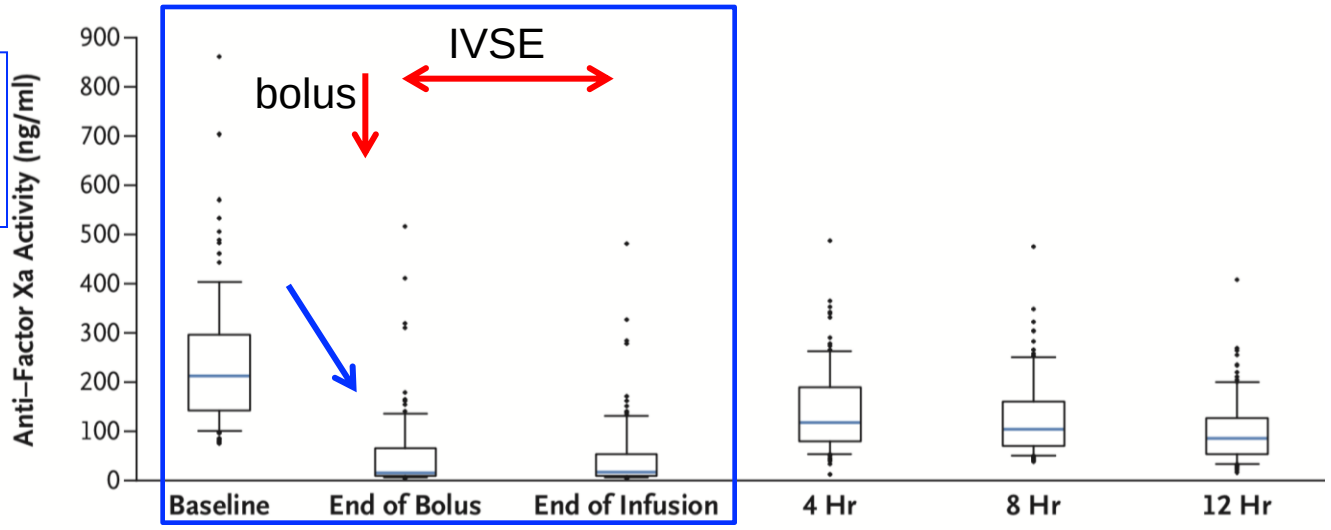

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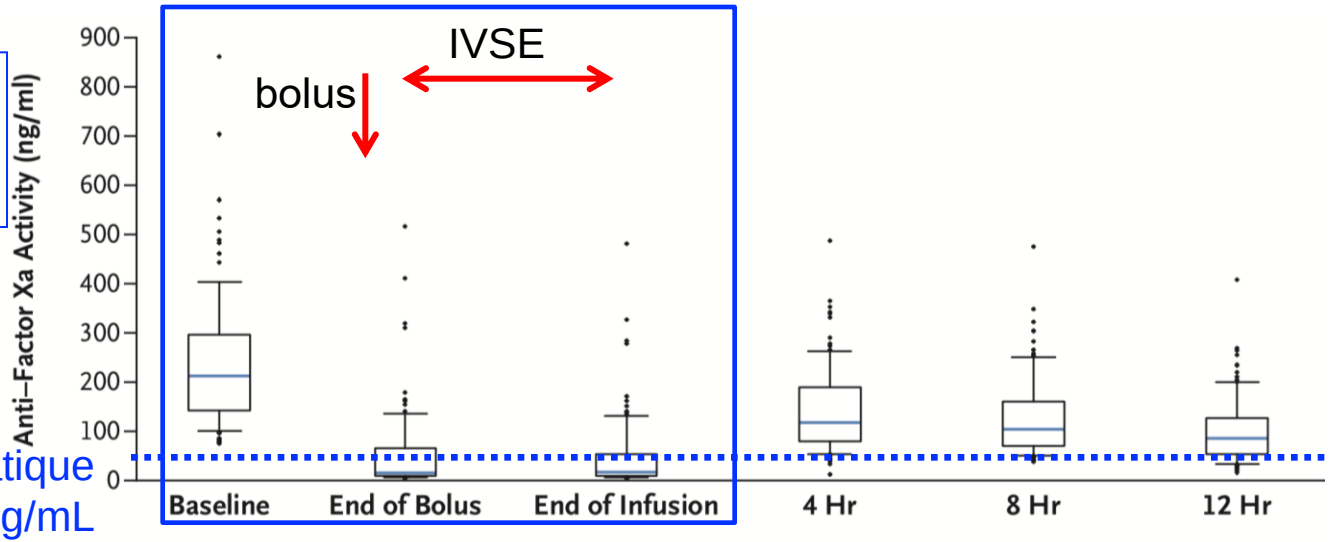

Seuil de sécurité hémostatique
50 ng/mL

Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors

ANNEXA-4 Investigators
February 7 2019

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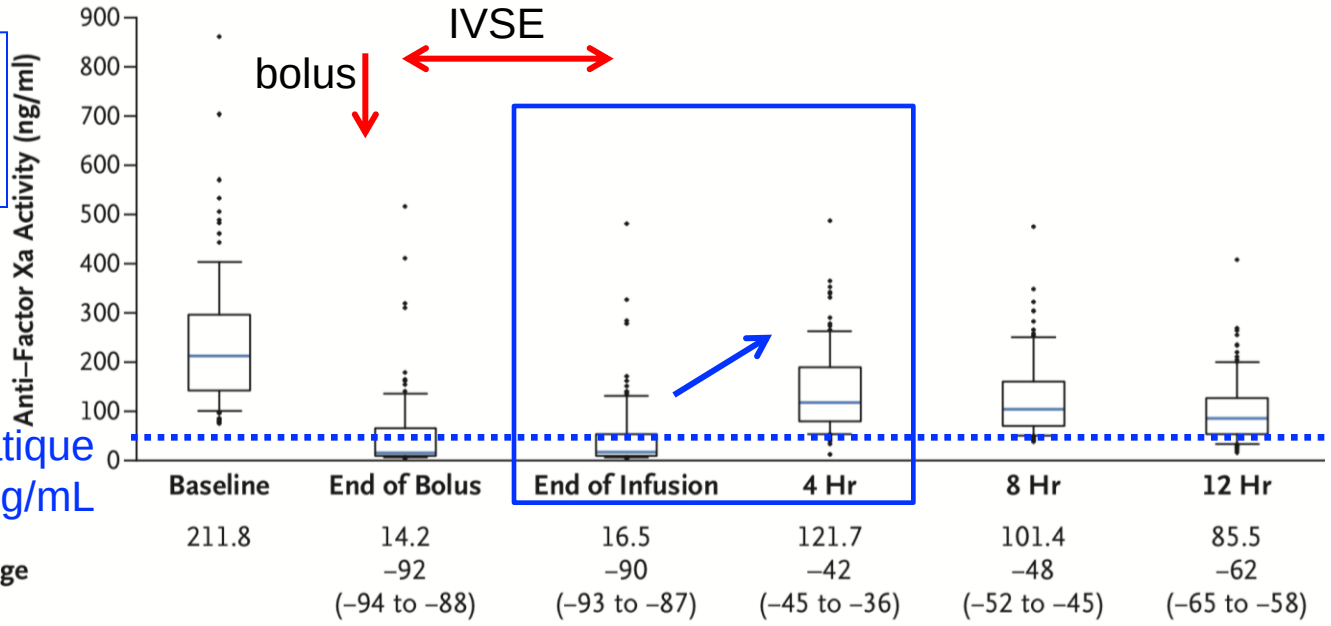

Seuil de sécurité hémostatique
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Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors

ANNEXA-4 Investigators
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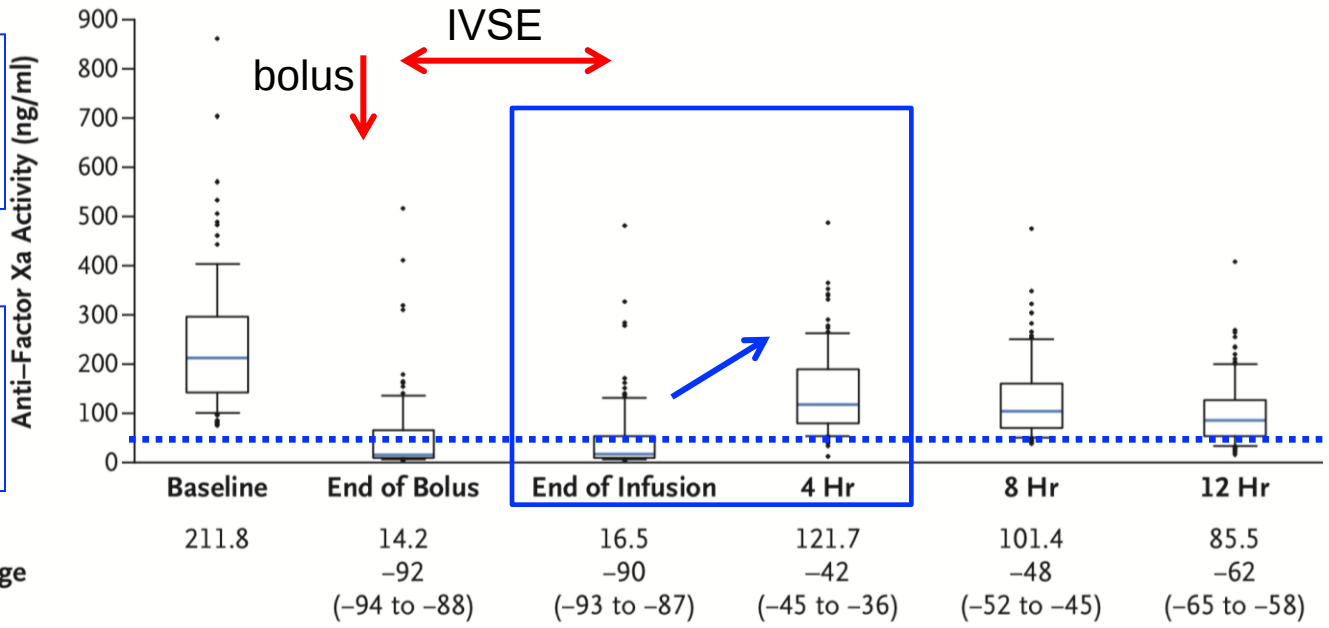
Rivaroxaban
>75 ng/mL
n=100

Evènements thromboemboliques
10% à 30 jours



NCT03661528

Trial of Andexanet in ICH Patients Receiving an Oral FXa Inhibitor

?

Andexanet for Factor Xa Inhibitor–Associated Acute Intracerebral Hemorrhage

Connolly SJ, Sharma M, Cohen AT (…) ANNEXA-I Investigators

2024

patients with ICH
<6 hrs of symptoms onset
<15 hrs oral FXa inhibitors

- Andexanet
- Usual Care

85.5% PCC

Primary endpoint: hemostatic efficacy **H12** postrandomisation
expansion of the hematoma volume ≤35%
↗ in the score on the NIHSS <7 points
no receipt of rescue therapy between 3 -12 hours

Safety: Thrombotic events
Death

Andexanet for Factor Xa Inhibitor–Associated Acute Intracerebral Hemorrhage

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2024

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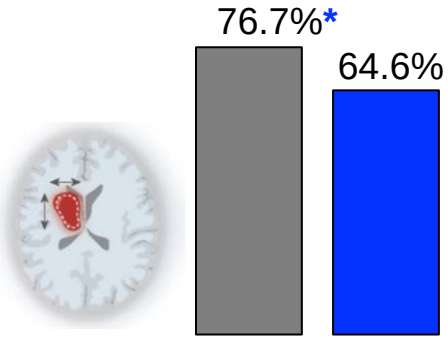
↗ in the score on the NIHSS <7 points
no receipt of rescue therapy between 3 -12 hours

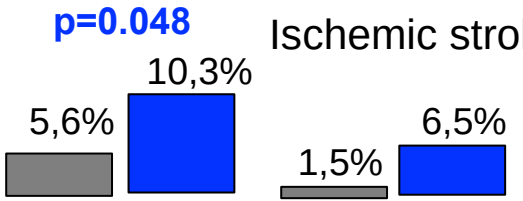
67 vs 53.1% adjusted difference, 13.4; 95%CI 4.6 to 22.2; **p=0.003**

Safety: Thrombotic events
Death

Hematoma volume Expansion



Thrombotic event



modified Rankin scale
Death within 30 days

No difference

Prothrombin complex concentrates

non activated PCC

Coagulation factors
II, VII, IX and X
(+/- protein C, S antithrombin, heparin…)

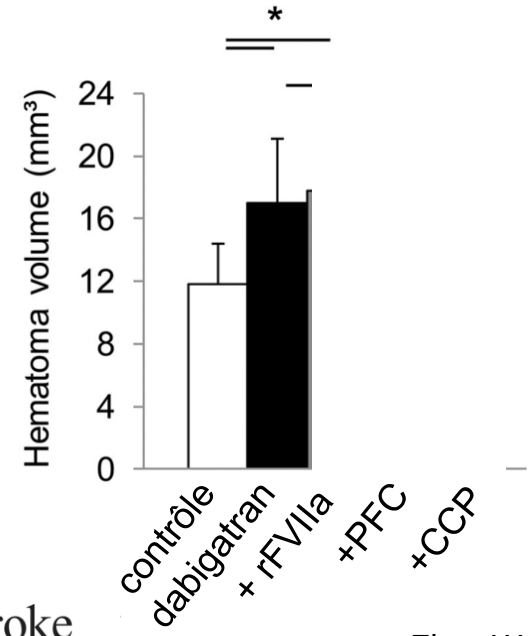
Activated PCC

Factor Eight Inhibitor By-passing Activity

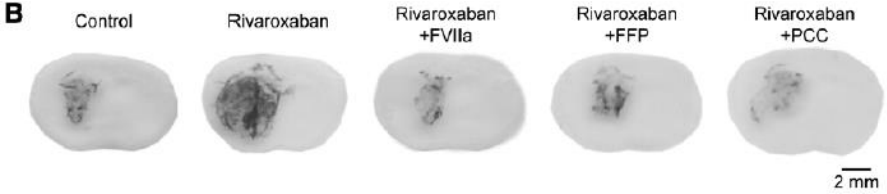
Mixture of coagulation factors
Including II, VII, IX and X
Including activated factors, mainly VIIa and IIa

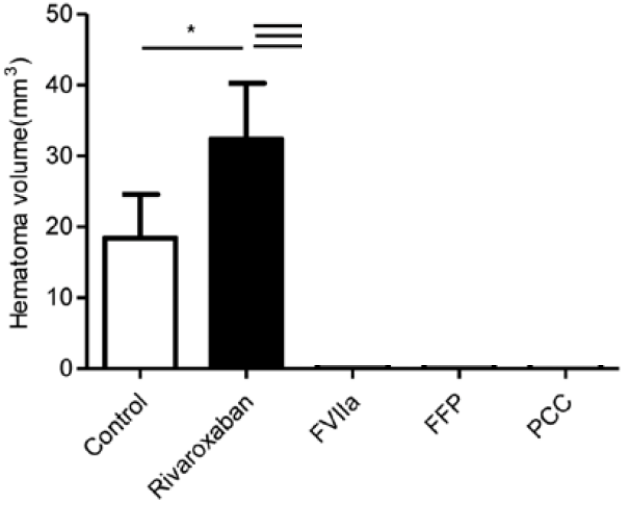
AOD et hématome intracérébral

Dabigatran



Rivaroxaban





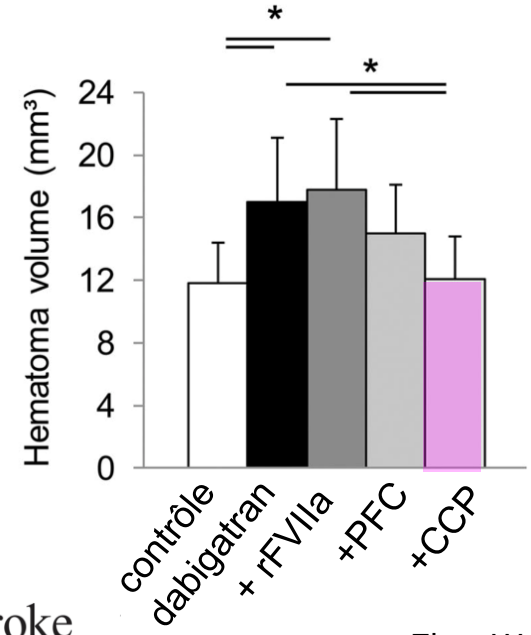
Stroke
Journal of the American Heart Association

Zhou W. Stroke 2011

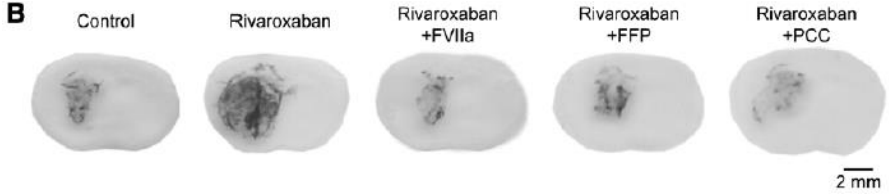
Zhou W. Stroke 2013

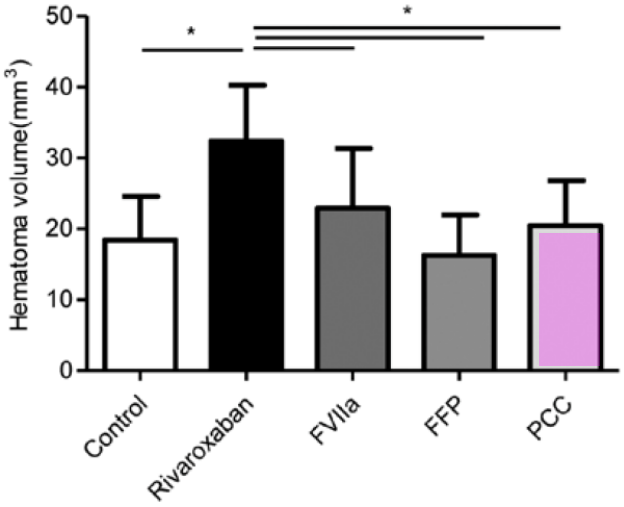
AOD et hématome intracérébral

Dabigatran



Rivaroxaban





Stroke
Journal of the American Heart Association

Zhou W. Stroke 2011

Zhou W. Stroke 2013

Prothrombin Complex Concentrate vs Conservative Management in ICH Associated With Direct Oral Anticoagulants

JAMA Network Open 2024

Ip B, Pan S, Yuan Z, Hung T, Ko H, Leng X, Liu Y, Li S, Lee SY, Cheng C, Chan H, Mok V, Soo Y, Wu X, Lui LT, Chan R, Abrigo J, Dou Q, Seiffge D, Leung T.

232 patients with DOAC associated ICH → propensity score–weighted retrospective cohort study → 25 to 50 IU/kg PCC / No hemostatic agents → mRS of 0 to 3 at 3 months, Mortality at 90 days, in-hospital mortality, hematoma expansion

	Prothrombin complex concentrate (n = 85) vs conservative management (referent, n = 97)	
Outcomes	**aOR (95% CI)**	***P* value**
Good neurological recovery at 90 d	0.62 (0.33-1.16)	.14
Mortality at 90 d	1.03 (0.70-1.53)	.88
In-hospital mortality	1.11 (0.69-1.79)	.66
Hematoma expansion[a]	0.94 (0.38-2.31)	.90

inefficace, infructueux, stérile, vain, dispensable, superfétatoire

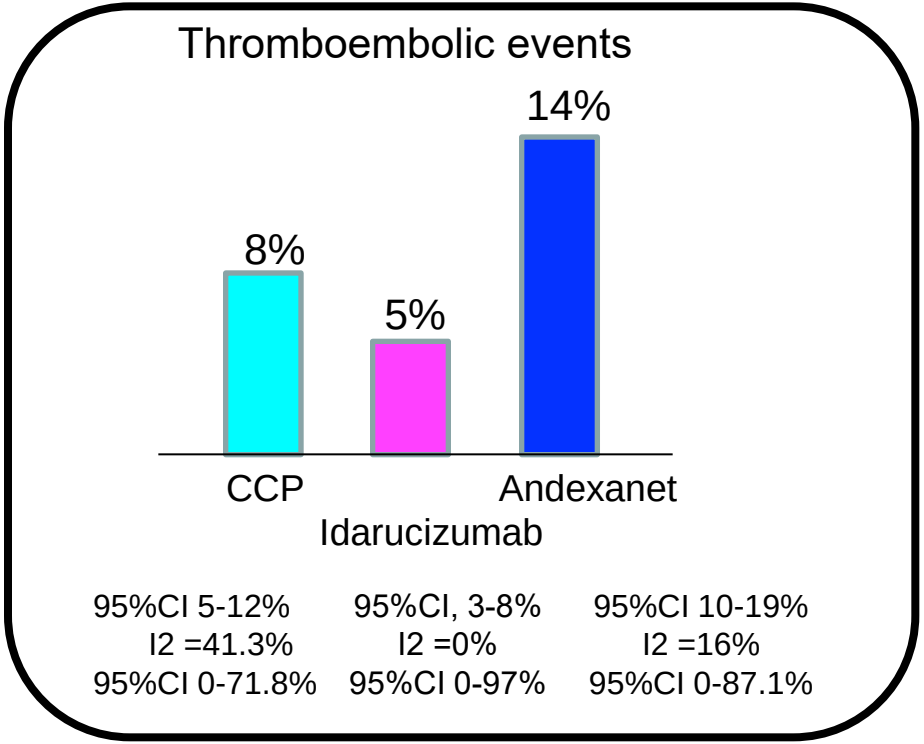
Evaluation of Direct Oral Anticoagulant Reversal Agents in Intracranial Hemorrhage

A Systematic Review and Meta-analysis

Chaudhary R, et al.

JAMA Network Open 2022

36 studies
1832 patients: 967 receiving 4-factor PCC
525 andexanet alfa
340 idarucizumab

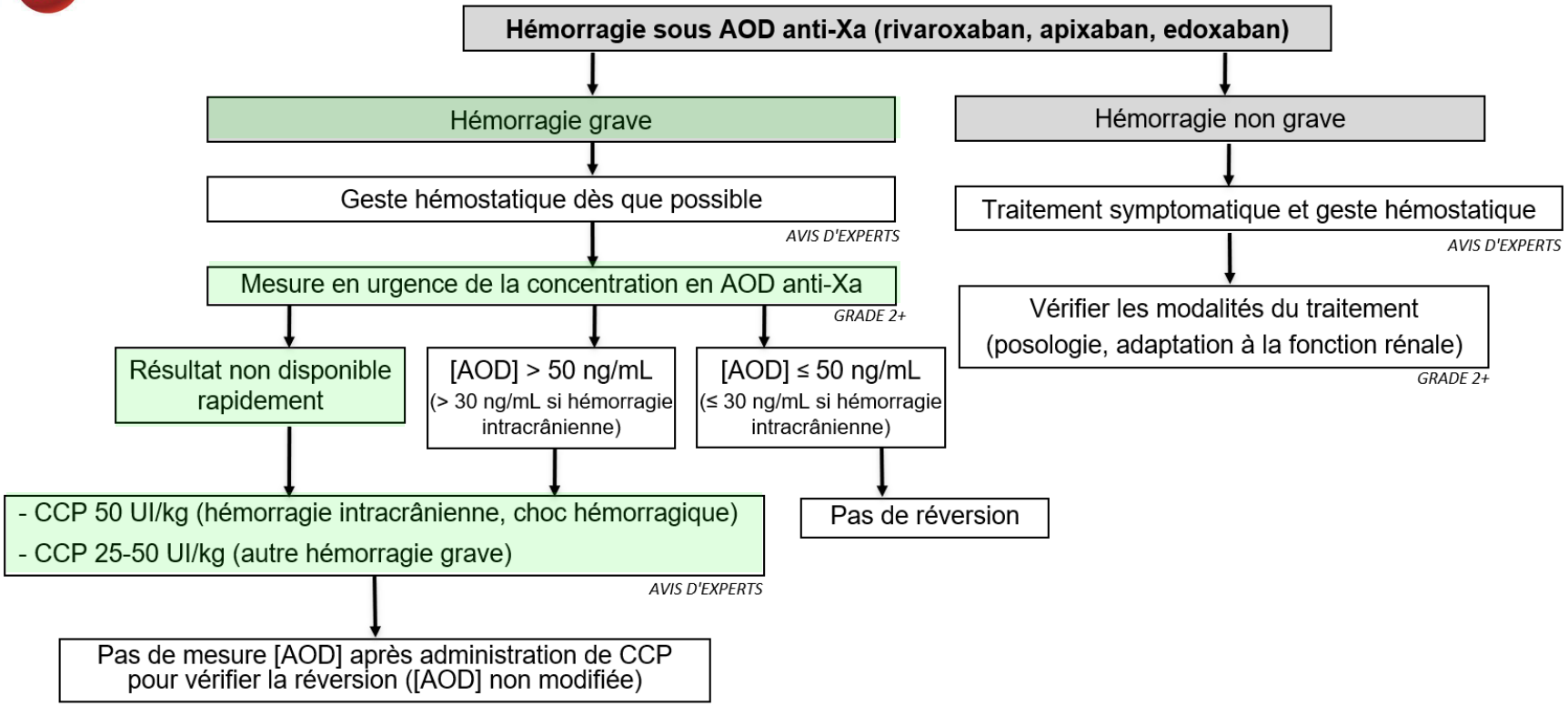


RFE 2024

SFAR SFMU Société Française de Médecine d'Urgence

SFTH SOCIÉTÉ FRANÇAISE DE THROMBOSE ET D'HÉMOSTASE

GIHP Groupe d'intérêt en hémostase péri-opératoire



RECOMMANDATIONS FORMALISÉES D'EXPERTS

De la **Société Française de Médecine d'Urgence,**

la **Société Française d'Anesthésie-Réanimation et médecine péri-opératoire**

du Groupe d'intérêt en Hémostase Péri-opératoire

et **Société Française de Thrombose et d'Hémostase**

Gestion de l'anticoagulation dans un contexte d'urgence

2024

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