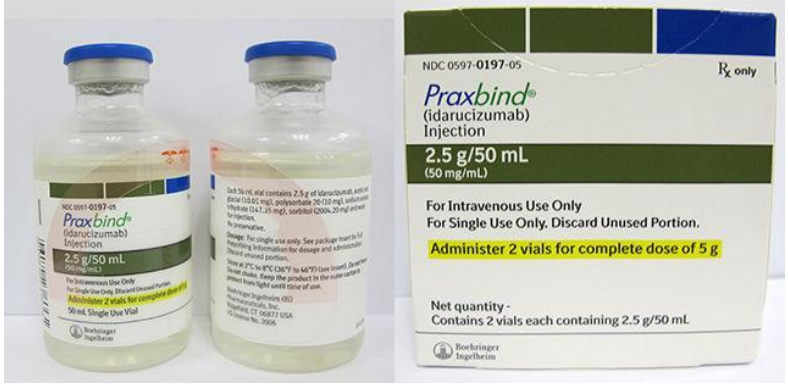
Praxbind反轉劑之介紹與使用

(腦中風中心系列課程)

蔡易訓 臨床藥師CP3

編　　號 P6A922P
藥　　名 Idarucizumab 2.5g/50ml/vial *2 /SET
英文商品名　Praxbind
中文商品名　達栓普注射液/輸注液
製造廠 BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG



適應症：

Praxbind屬於一種專一性的dabigatran反轉作用劑，適用於接受普栓達(Pradaxa)治療而需要快速反轉dabigatran抗凝血作用的成人病患：

1.供緊急手術/緊急程序(urgent procedures)使用。
2.於威脅生命或控制不良的出血時使用。

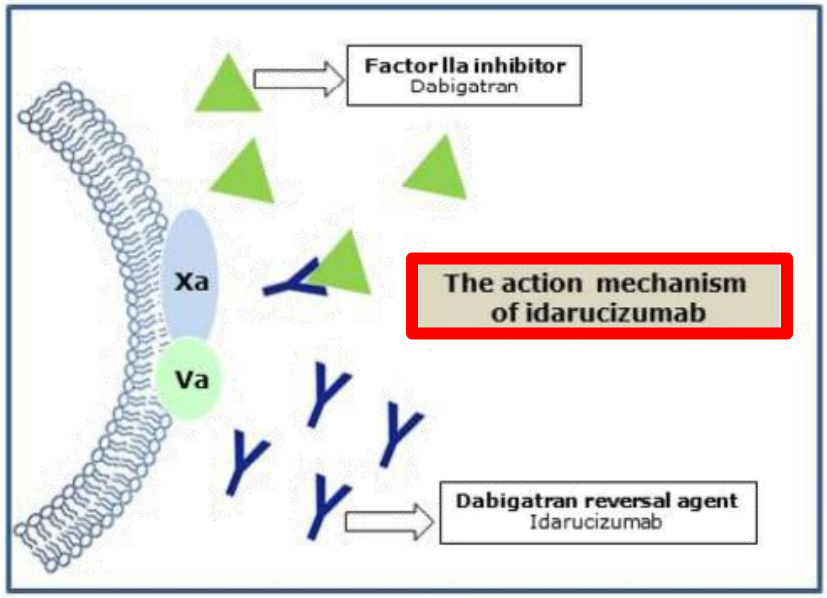
用法用量：

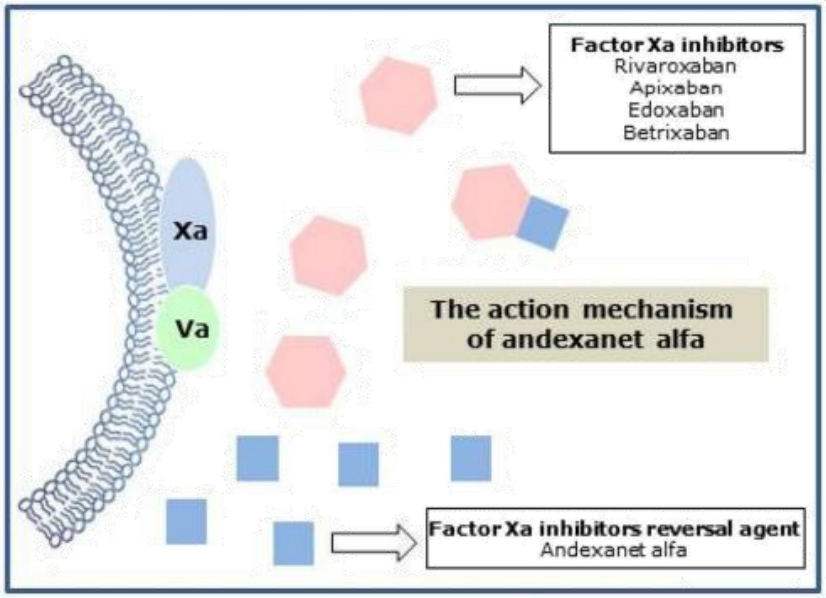
建議劑量為5g (2×2.5g/50ml)，以靜脈注射方式施用 (不需稀釋)。
兩個vial各於5-10分鐘內完成連續輸注 或是 快速靜脈注射。

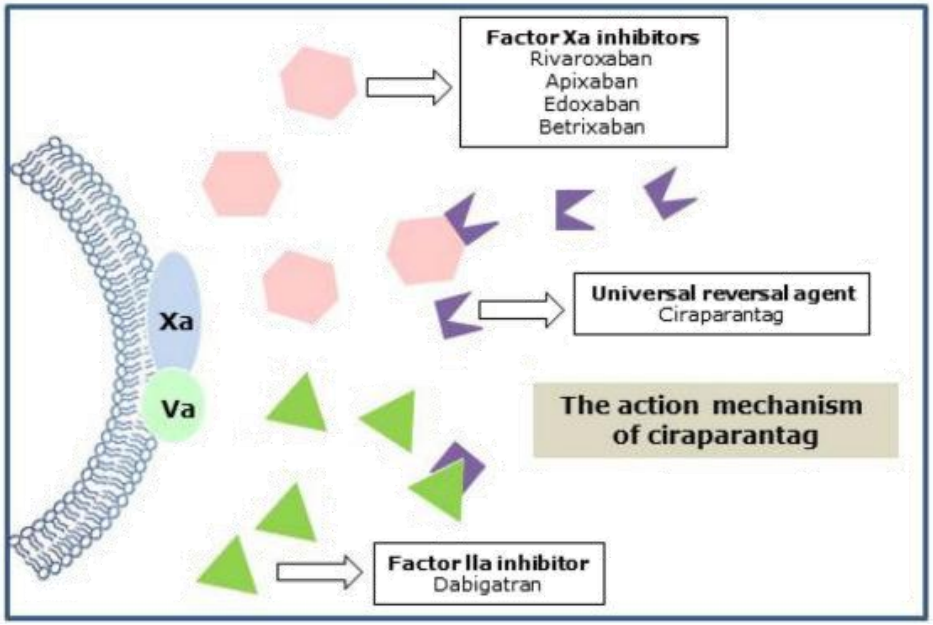
禁忌症：無。

注意事項：

1. **Praxbind不得與其他藥物混合，且同一時間勿以同一靜脈管路實施其他輸注。**
2. **Praxbind不含防腐劑僅供單次使用，於室溫下物化性質穩定時間為6小時。**







Praxbind (Idarucizumab)為dabigatran專一性反轉劑

Zhao S et al. Am J Cardiovasc Drugs (2020)

Idarucizumab is easy to administer and has no contraindications

Idarucizumab 5 gram IV*

Idarucizumab is administered as a fixed dose, regardless of the clinical situation

Vials contain a ready-mixed solution for administration

Infuse intravenously

The complete 5 gram dose should be given as two consecutive IV infusions over 5–10 minutes each

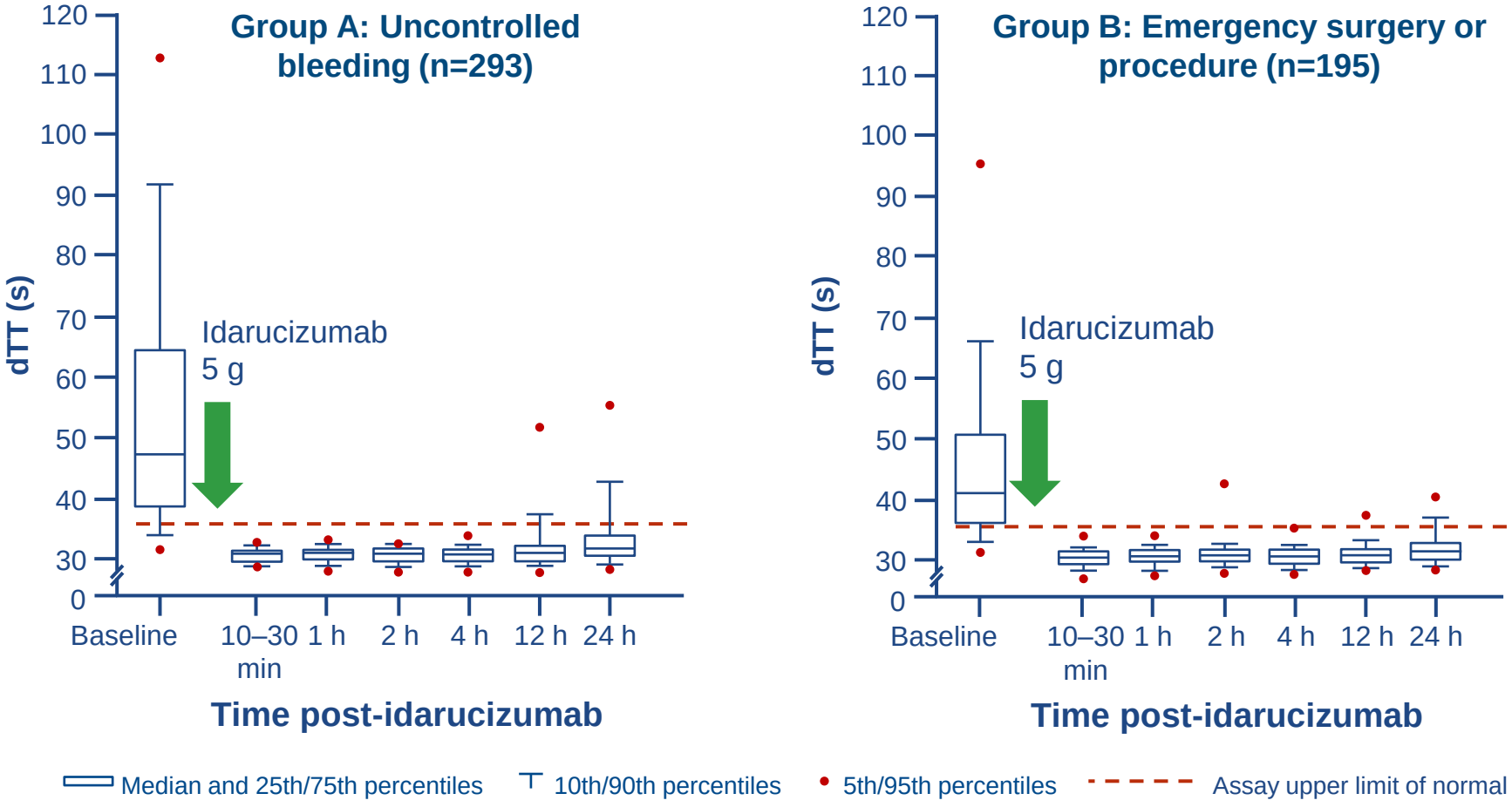
OR

Inject intravenously

Give the complete 5 gram dose in two separate consecutive bolus injections

No need for anticoagulation tests prior to administration or between vials

RE-VERSE AD: idarucizumab provided immediate, complete, and sustained reversal of dabigatran anticoagulation, based on dTT

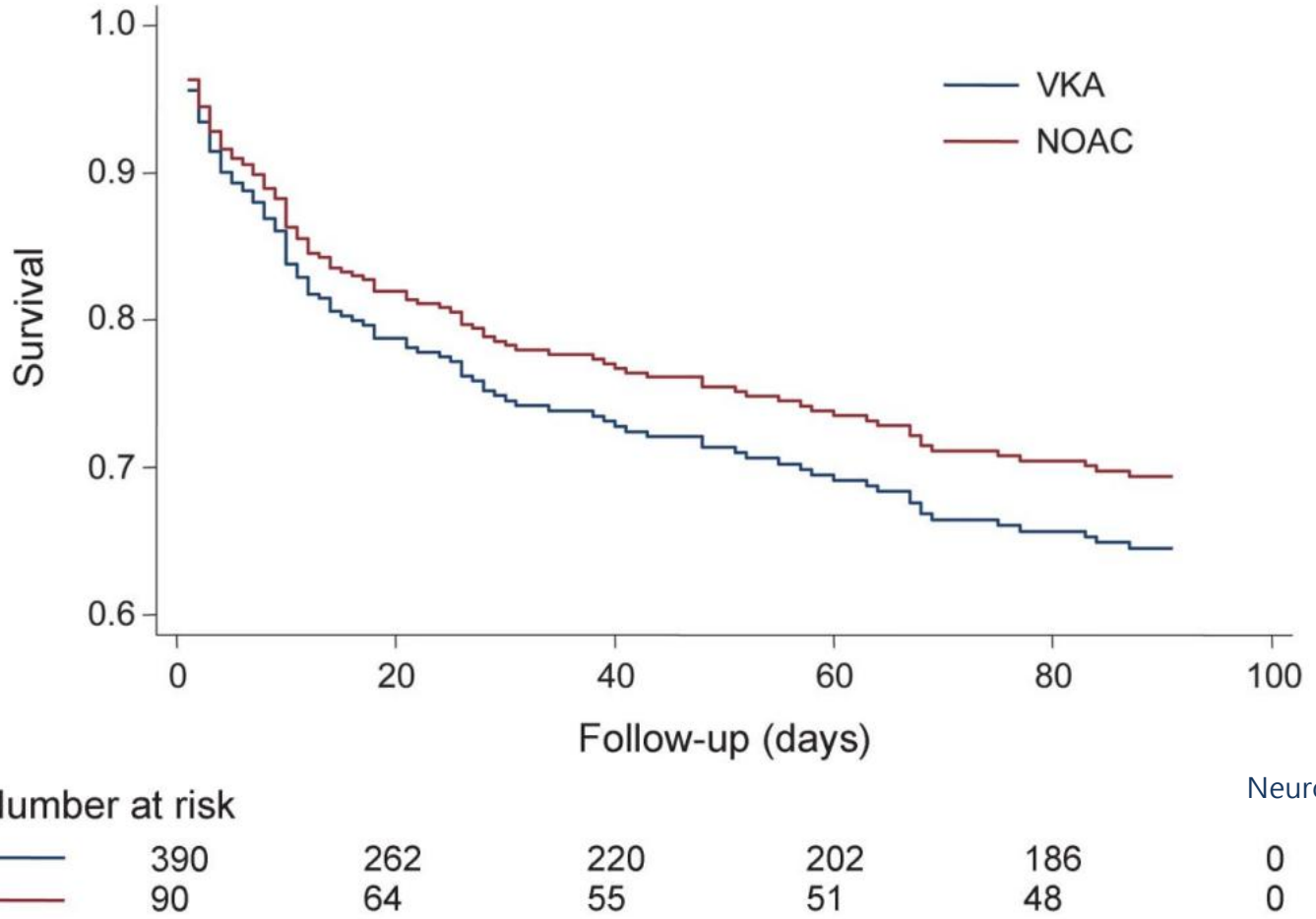


Praxbind注射後，可於10分鐘內反轉dabigatran抗凝血效果

dTT, diluted thrombin time

Pollack et al. N Engl J Med 2017

Survival curve comparing non–vitamin K oral antagonist anticoagulant (NOAC)–associated intracerebral hemorrhage (ICH) and vitamin K antagonist anticoagulant (VKA)–associated ICH 90-day mortality

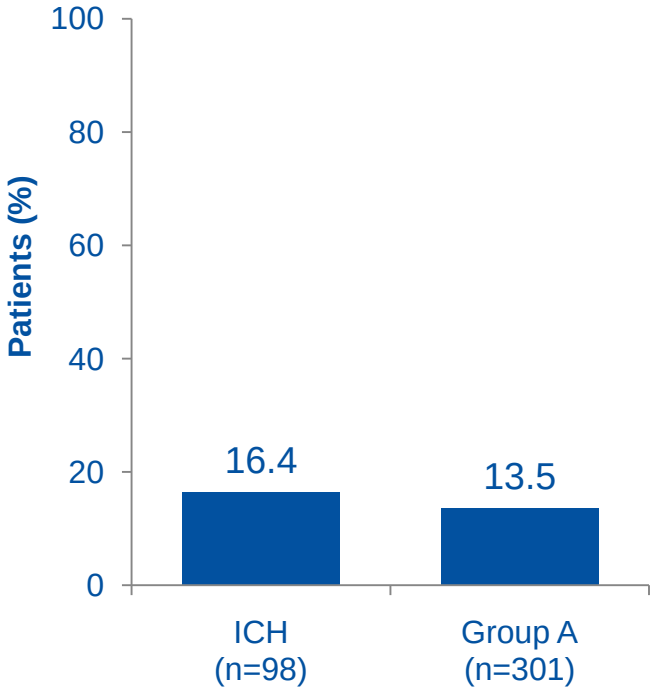


Neurology 2017; 88:1693

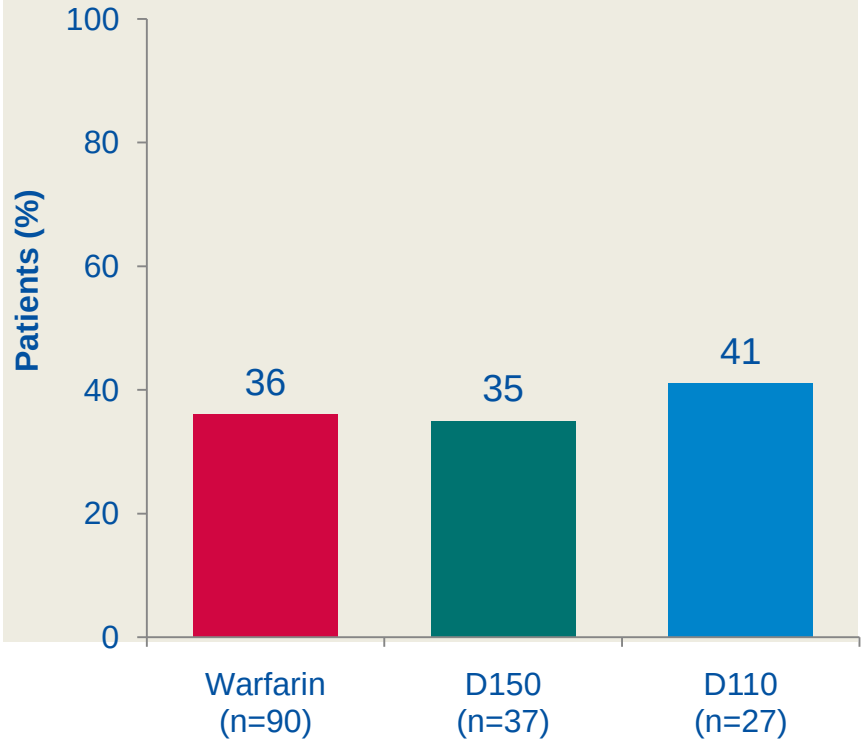
	NOAC-ICH patient (N=100)	VKA-ICH (N=440)
90d-Mortality	33%	31%
Hematoma Expansion >33% or 6 ml	40%	34%

RE-VERSE AD: 98 patients with ICH
30-day mortality

Mortality due to ICH in RE-VERSE AD™[1]



Mortality due to all types of ICH in RE-LY®[2]

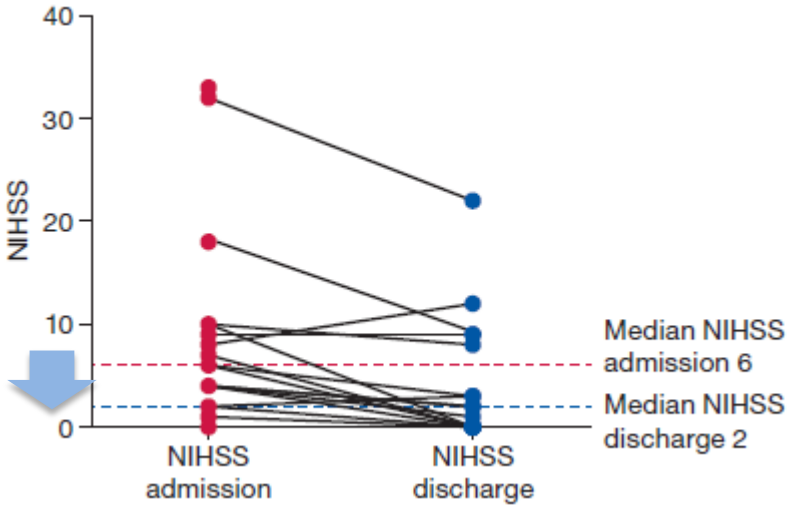


Praxbind 可降低使用dabigatran使用後造成顱內出血死亡率

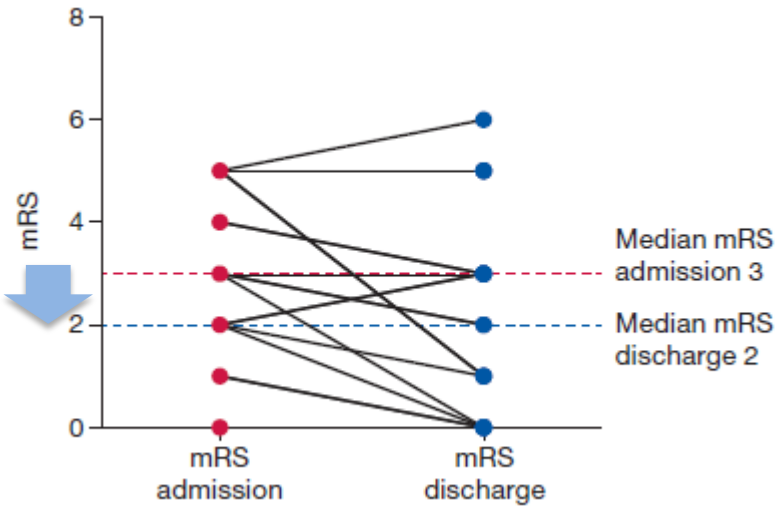
Data for mortality due to ICH in RE-LY comes from a historical cohort. No clinical conclusions can be drawn from this comparison
D150, dabigatran 150 mg BID; D110, dabigatran 110 mg BID; 1. Pollack et al. New Engl Med J 2017; 2. Hart et al. Stroke 2012

Most ICH patients experienced improvement in neurological status and physical function after idarucizumab administration

**NIHSS score*
(stroke severity)**



**mRS score
(disability)**



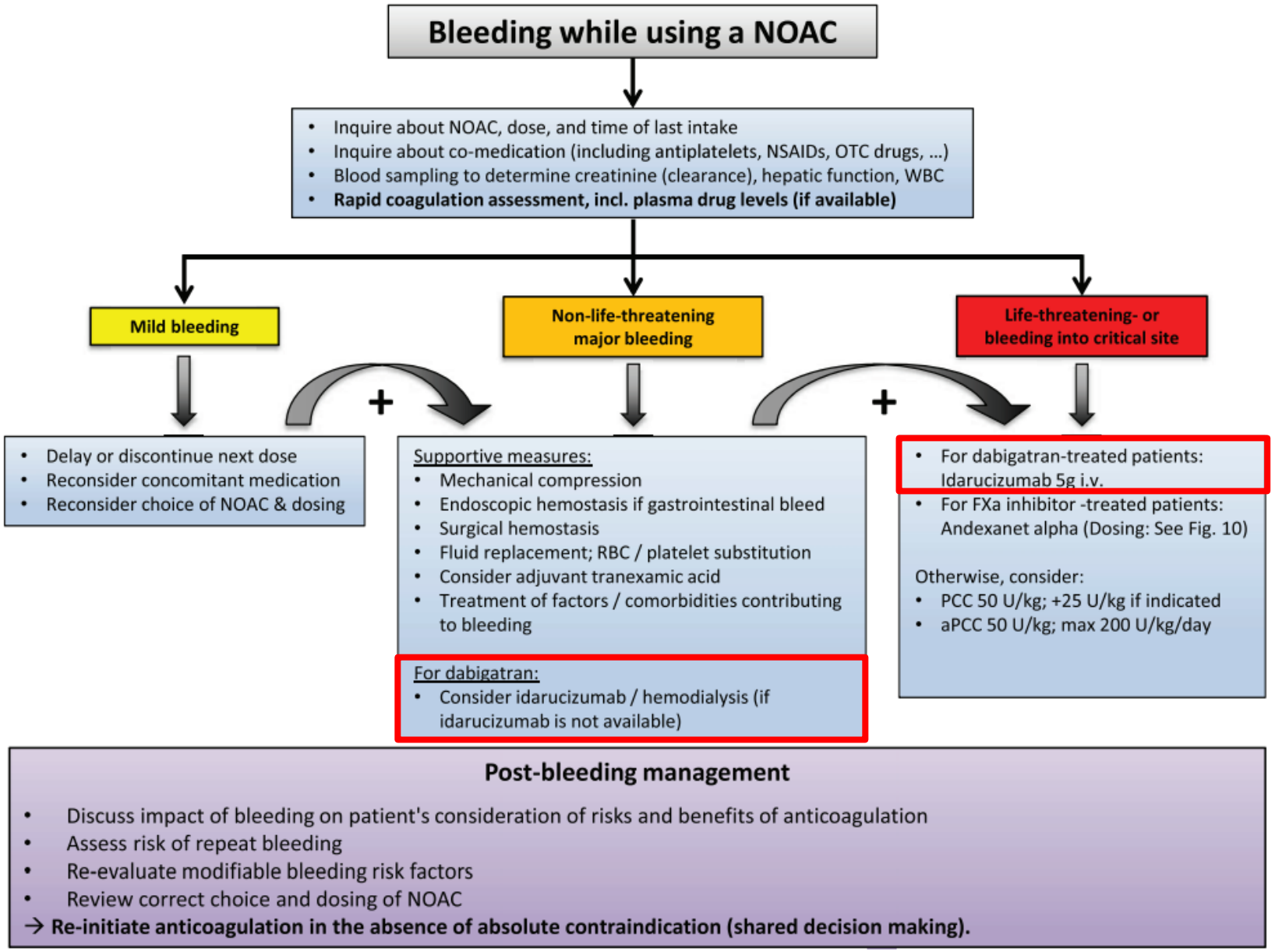
No Hematoma growth in 78.94%(15/19)

As it has the potential to prevent haematoma growth, reversing anticoagulation with idarucizumab may have aided neurological and functional improvement

*The NIHSS score for two patients at admission and one patient at discharge was not available

Grond M et al. ESOC 2017

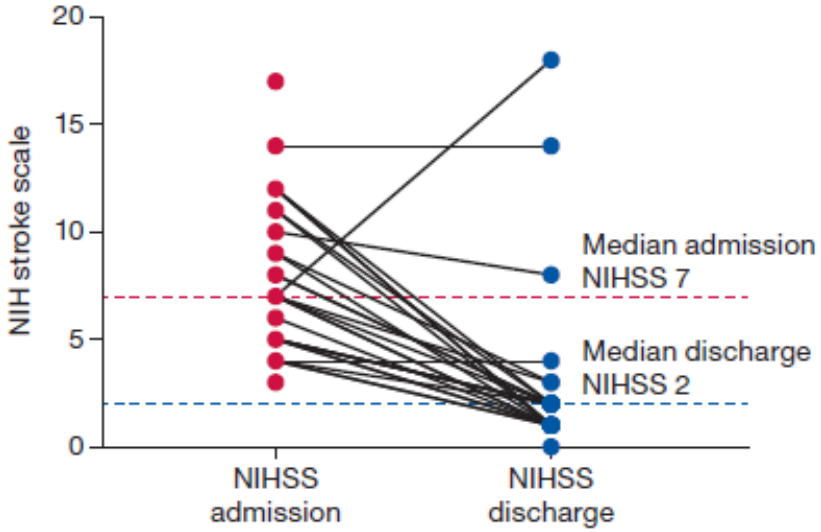
2021 EHRA Practical Guide:
Management of bleeding in patients taking NOACs



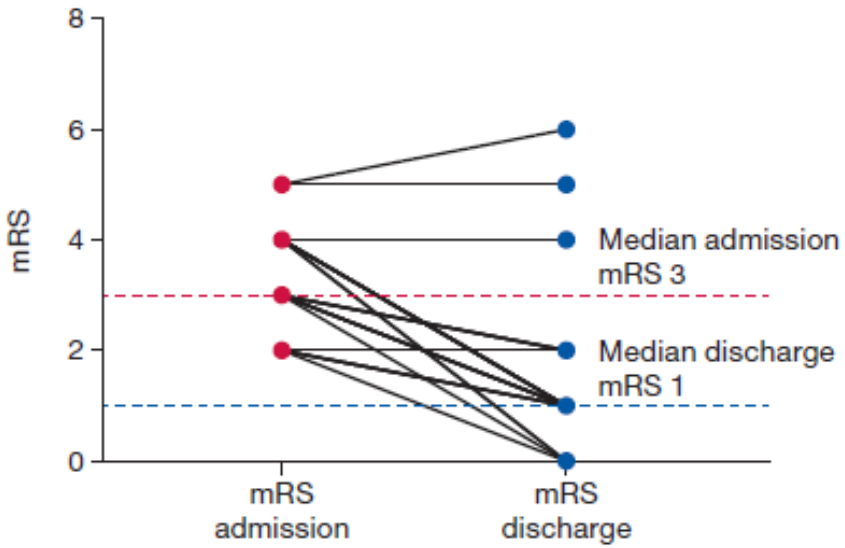
Most patients experienced improvement in neurological status and physical function after thrombolysis following idarucizumab administration

Ischaemic stroke

NIHSS score* (stroke severity)



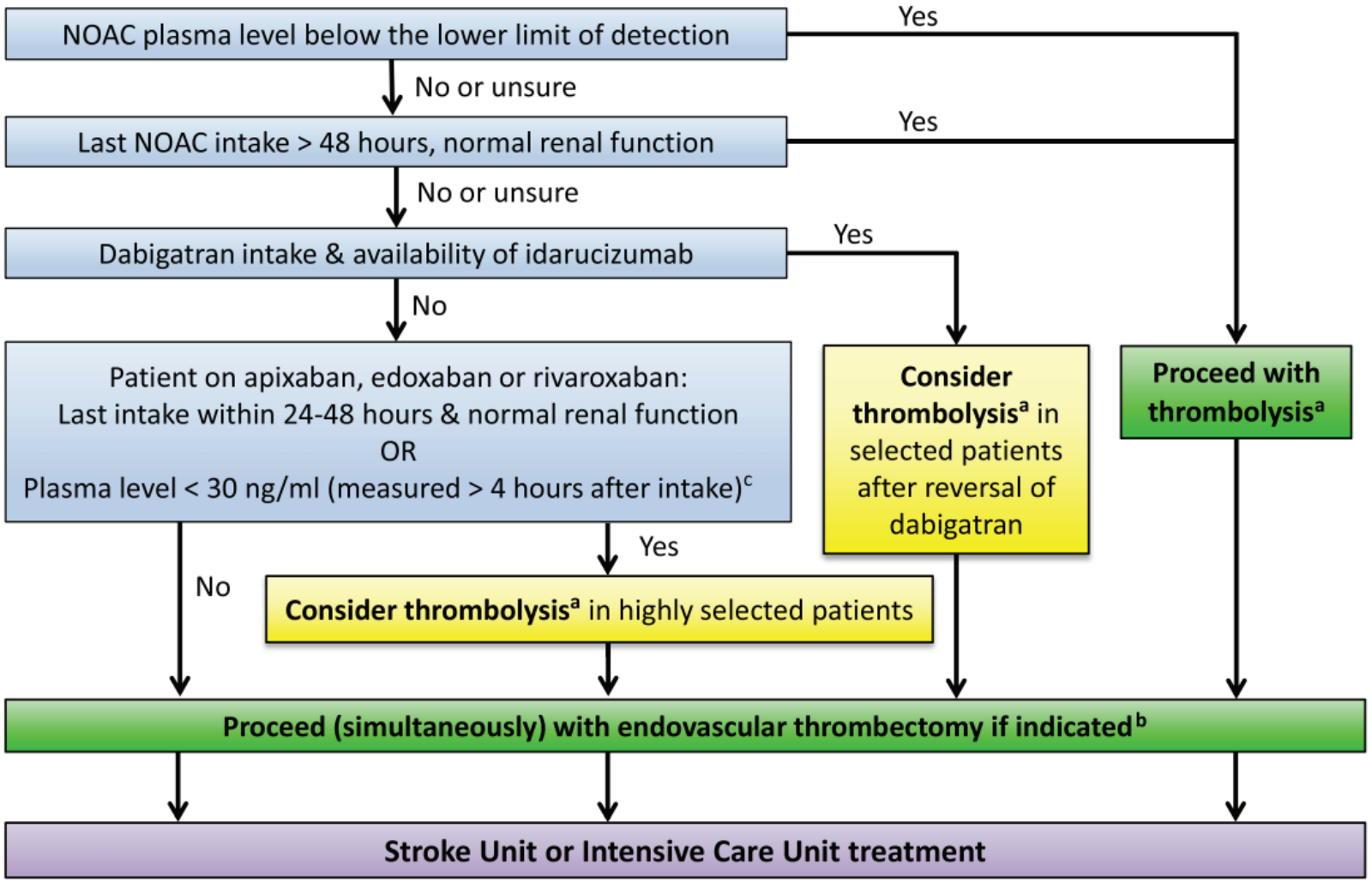
mRS score (disability)



No hemorrhagic transformation. 1 patient expired due to PE two weeks later. (anticoagulation had not been restarted)
NIHSS from 7 to 2. 86.67%(26/30) individuals benefitted from intravenous thrombolysis at discharge

The NIHSS score was not available for two patients at discharge
mRS, modified Rankin Scale; NIHSS, the National Institutes of Health Stroke Scale
Diener H-C et al. ESOC 2017

Acute management of acute ischaemic stroke in a patient on NOACs: Currently only available for dabigatran (idarucizumab) can consider thrombolysis treatment



Praxbind enhance Pradaxa safety benefit based on Taiwan real-world experiences

Case Studies

Real-World Experience with Idarucizumab to Reverse Anticoagulant Effect in Dabigatran-Treated Patients: Report of 11 Cases from Taiwan

Li-Kai Tsai, MD, PhD,* Huey-Juan Lin, MD, MPH,† Su-Kiat Chua, MD, PhD,‡ Pen-Chih Liao, MD,§ Yuan-Po Yang, MD,‖ Ping-Chen Chou, MD,¶ Chun-Wei Lee, MD,# Mao-Jen Lin, MD, PhD,** Hsi-Ming Chen, MD,†† Jung-Tze Yeh, MS,‡‡ and Yi-Heng Li, MD, PhD§§

Background: This study aims to observe the effectiveness and safety of idarucizumab in dabigatran-treated patients with severe bleeding or requiring surgery in Taiwan. *Methods and Results:* In Taiwan, 11 dabigatran-treated patients developed severe bleeding, fracture that needed surgery, and acute ischemic stroke requiring thrombolysis. These patients were treated with idarucizumab and obtained adequate

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Formosa Journal of Clinical Pharmacy Vol. 26 No. 1(2018), pp. 75-79

Formosa J Clin Pharm

案例報告

以 Idarucizumab 及血栓溶解劑治療缺血性中風之案例報告

Management of Ischemic Stroke with Idarucizumab and Systemic Thrombolysis: Case Report

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Conclusions:

- ✓ **Real-world experiences reconfirm the efficacy of Praxbind and demonstrate its role in improving patient safety with dabigatran treatment.**
- ✓ **Continued education about appropriate use of Praxbind is necessary in Asia.**

Journal of Stroke and Cerebrovascular Diseases, Tsai LK et al., 2017 Nov.
Formosa Journal of Clinical Pharmacy Vol. 26 No. 1(2018), pp. 75-79

Intravenous Thrombolysis in Acute Ischemic Stroke After Idarucizumab Reversal of Dabigatran Effect: Analysis of the Cases From Taiwan

Table 2. *Clinical course, treatment, and outcome of cases from Taiwan, Japan, and Hong Kong*

Case no.	Time from last intake of dabigatran to admission (h)	Time from admission to idarucizumab (min)	Time from the end of idarucizumab injection to start rt-PA (min)	aPTT before idarucizumab (s)	aPTT after idarucizumab (s)	rt-PA dose (mg/kg)	ICH	NIHSS score at admission	NIHSS score at follow-up or discharge
1	12	133	10	24.6	n.a.	.6	No	12	12
2	2.5	90	10	36.1	n.a.	.7	No	12	10
3	24	41	17	n.a.	n.a.	.7	No	12	2
4	6	63	8	25.6	n.a.	.9	No	26	n.a.
5	7	25	n.a.	32.9	27.6	.9	No	16	10
6	16	28	19	26.8	n.a.	.9	Yes (S)	24	n.a. (mortality)
7	9	32	17	25.1	23.8	.9	Yes (A)	9	6
8	1.5	50	5	29.5	29.1	.6	No	19	16
9	9	79	8	42.9	26.2	.9	Yes (A)	23	14
10	n.a.	101	6	31.5	27.4	.7	No	7	5
Mean ± SD	9.67 ± 6.59	64.20 ± 34.06	11.11 ± 4.91	30.55 ± 5.72	26.82 ± 1.77	.78 ± .12		16.0 ± 6.67	9.38 ± 4.75
Japan	n.a.	39	rt-PA was given after idarucizumab infusion for 15 min	41.3	n.a.	n.a.	No	22	7
Hong Kong	2 h before onset	n.a.	rt-PA was given 10 min after the start of idarucizumab injection	50.7	29.5	.6	No	34	improved

A, asymptomatic; aPTT, activated partial thromboplastin time; n.a., not available; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue plasminogen activator; S, symptomatic; SD, standard deviation.

Fang, C.W. et al., Journal of Stroke and Cerebrovascular Diseases, in process. (Accepted in Dec. 2018)

Intravenous Thrombolysis in Acute Ischemic Stroke After Idarucizumab Reversal of Dabigatran Effect: Analysis of the Cases From Taiwan

- 10 dabigatran-treated patients (6 men, mean age 71.10 - 7.96 years)
- Before stroke, the mean CHA2DS2-VASc score was 4.50 § 1.57 and 8 patients (80%) received dabigatran 110 mg twice daily.
- All patients were treated with 5 g idarucizumab, following APTT normalized.
- Intravenous rt-PA (mean dose .78 mg/kg) was initiated a mean time of **11.11 minutes after idarucizumab infusion**.
- The NIHSS score improved significantly after thrombolysis (16.0 § 6.67 at admission to 9.38 § 4.75 at discharge, P = 0.016).
- 1 patient suffered from symptomatic ICH leading to mortality.

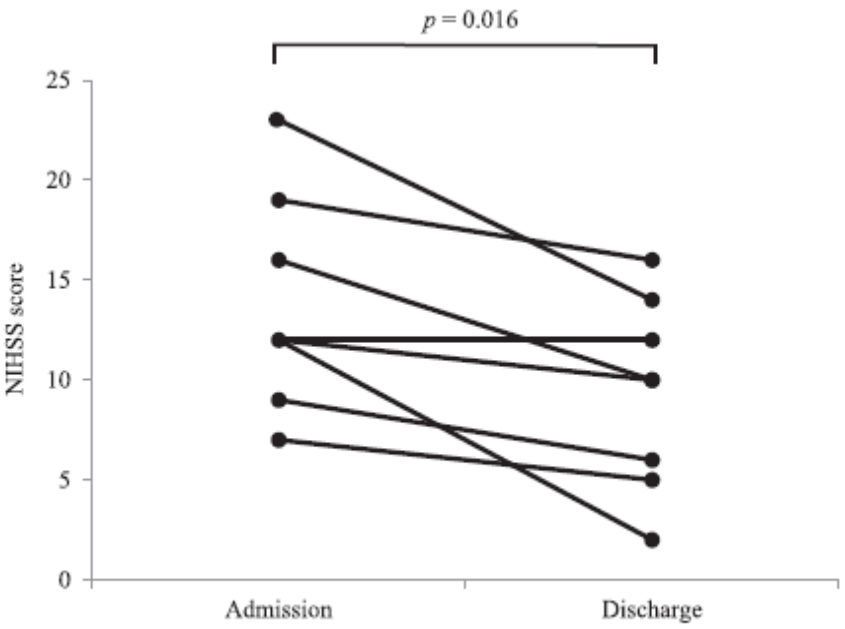

Figure 1. *The changes of the NIHSS score at admission and discharge. NIHSS, National Institutes of Health Stroke Scale.*

Fang, C.W. et al., Journal of Stroke and Cerebrovascular Diseases, in process. (Accepted in Dec. 2018)

1. 患者若在中風發生前48小時內曾服用 NOAC (dabigatran, rivaroxaban, apixaban, edoxaban)，則不建議施打血栓溶解劑 (Class III, Level of Evidence C-EO)，而此類患者若懷疑有特定大血管阻塞時，可考慮進行動脈內取栓術(Class IIb, Level of Evidence B-NR)。至於服用 dabigatran 的患者，可考慮使用反轉劑idarucizumab 後再施打血栓溶解劑 (Class IIb, Level of Evidence C-EO)。

2. 接受dabigatran而發生嚴重出血的患者， 應考慮經靜脈注射idarucizumab 5g反轉 dabigatran的抗凝血效果(Class I, Level of Evidence B-NR)。