RAPIDO

Preliminary results from a UK-wide audit of reversal agents for direct oral anticoagulant associated bleeding

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Aim: Audit the use of reversal agents for DOAC-associated bleeding across the UK

Background

- Major bleeding is a frequent complication of anticoagulation with direct oral anticoagulants
- Reversal agents are available but there are limited data on their use across the UK and whether this use is appropriate
- Although there is compelling data supporting the notion that these therapies are physiologically active, data on true clinical benefit is extremely limited
- UK-wide, patient level data is required to understand the current use of these agents

Results

81 Median age | 58% Male | 75% White

83% Atrial fibrillation | 18% Venous thrombosis | 29% Arterial thrombosis

49 (6%) Andexanet alfa | 47 (6%) Idarucizumab | 327 (39%) Beriplex | 414 (50%) Octaplex

93% Major haemorrhage | 41% 90-day mortality | 4% 90-day thrombosis

	N=837	%
Age (mean, SD)	79.0 (10.6)	
Male	487	58.2
Ethnicity: white	625	74.7
Comorbidities		
Atrial fibrillation	699	83.5
Cancer	120	14.3
Dementia	121	14.5
Falls	217	25.9
Heart failure	210	25.1
Ischaemic heart disease	195	23.3
Liver disease	58	6.9
Prior arterial thrombosis	246	29.4
Prior major bleeding	70	8.4
Prior venous thrombosis	154	18.4
Concurrent medications		
Antihypertensives	566	67.6
Antiplatelets	90	10.8
SSRI	89	10.6
PPI	354	42.3
Anticoagulant		
Apixaban	448	53.5
Dabigatran	52	6.2
Edoxaban	77	9.2
Rivaroxaban	260	31.1
Anticoagulant dose		
Low dose	283	33.8
Standard	515	61.5
Loading dose	7	0.8
Other	32	3.8

Table 1. Demographic and clinical information

Dosing

Andexanet alfa
High dose: 7 (14%)
Low dose: 42 (86%)

Idarucizumab
5g: 47 (100%)
Second dose: 1 (1%)

PCC (beriplex and octaplex)
Off-licence use
Recommended dose caps
Beriplex 5,000, Octaplex 3,000 units
1% doses exceeded caps

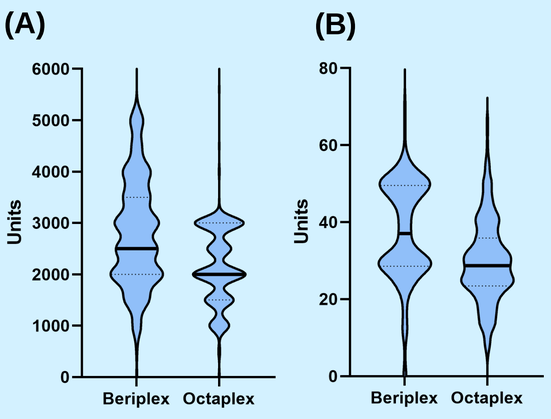

Figure 2. Dosing of beriplex and octaplex. (A) Total dose (B) Dose per kg.

Methods

- RAPIDO is a UK-wide retrospective audit collecting data from routine patient records.
- Inclusion criteria:
  - *Age ≥ 18 years*
  - *Administration of 4 factor prothrombin complex concentrate (PCC [beriplex or octaplex], andexanet alfa or idarucizumab)*
  - *Between 1st October 2020 and July 31st 2023 (current data until Jan 31st 2022)*
- Data is collected by HaemSTAR collaborators - doctors and allied health professionals
- Data is anonymised and entered into a secure, online REDCap database
- Data has been analysed in GraphPad Prism 9
- The audit was supported by funding from AstraZeneca UK Limited

Primary outcomes

- Proportion of patients treated with a reversal agent who had severe or life-threatening bleeding
- Proportion of patients treated with a reversal agent who received treatment in accordance with the dosing schedule laid out in the relevant SPC

Bleed sites

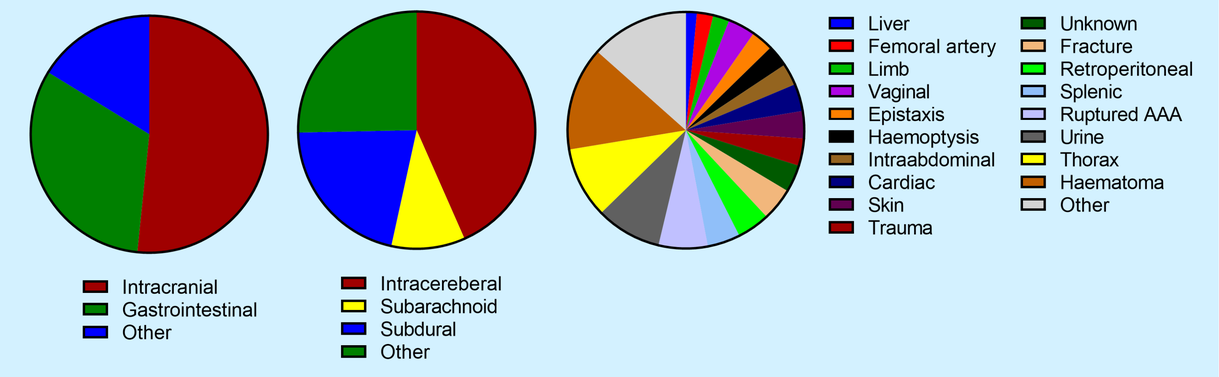

Figure 1. Anatomical sites of bleeding. (A) All patients (B) Sites of intracranial bleeds (C) Sites of "Other" bleeding.

Clinical outcomes

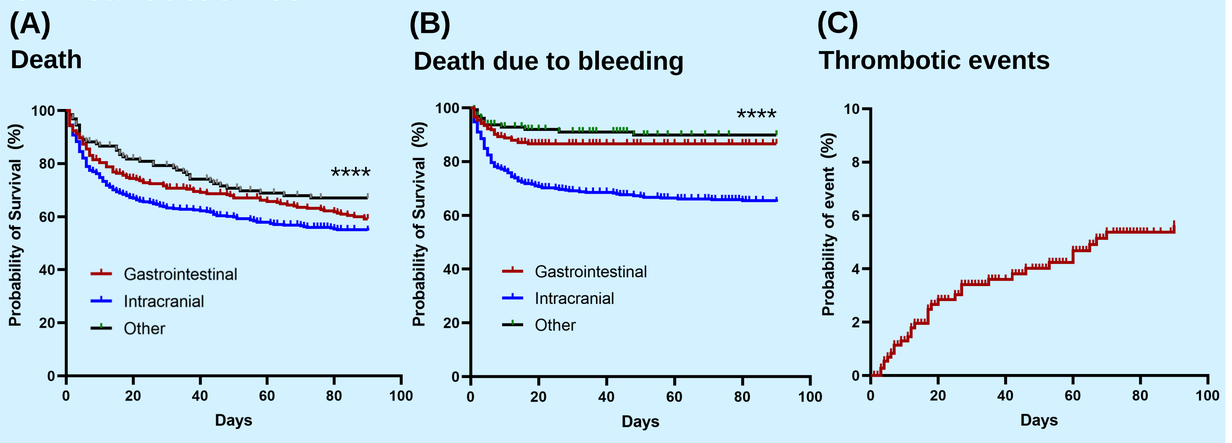

Figure 3. Clinical outcomes. Kaplan-Meier analyses of (A) death by bleed site, (B) death due to bleeding by bleed site, and (C) incidence of thrombosis. ****P<0.0001 for significance of difference by log rank test.

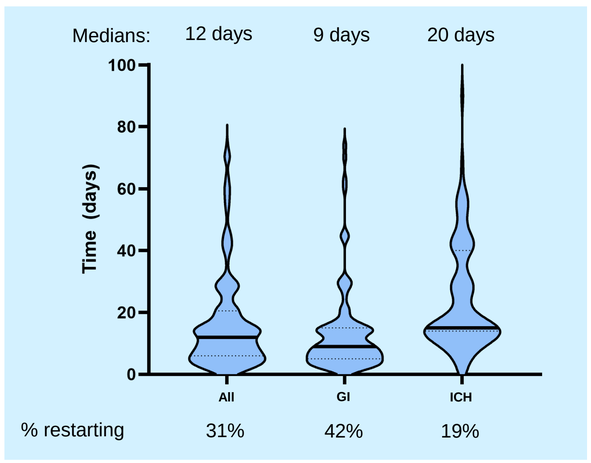

Figure 4. Timing of restarting anticoagulation

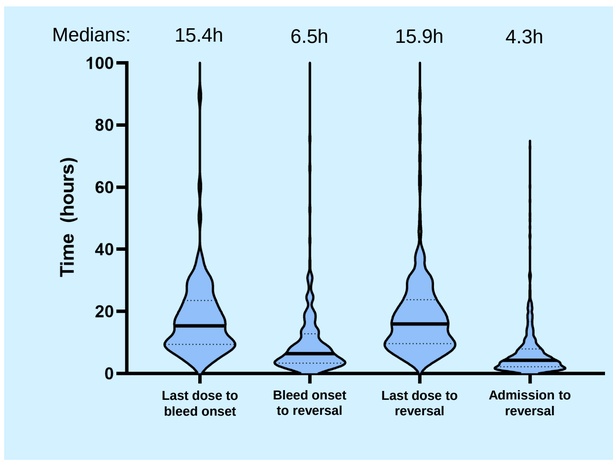

Figure 5. Time between events (hours)

Clinical outcomes: PCC (beriplex and octaplex)

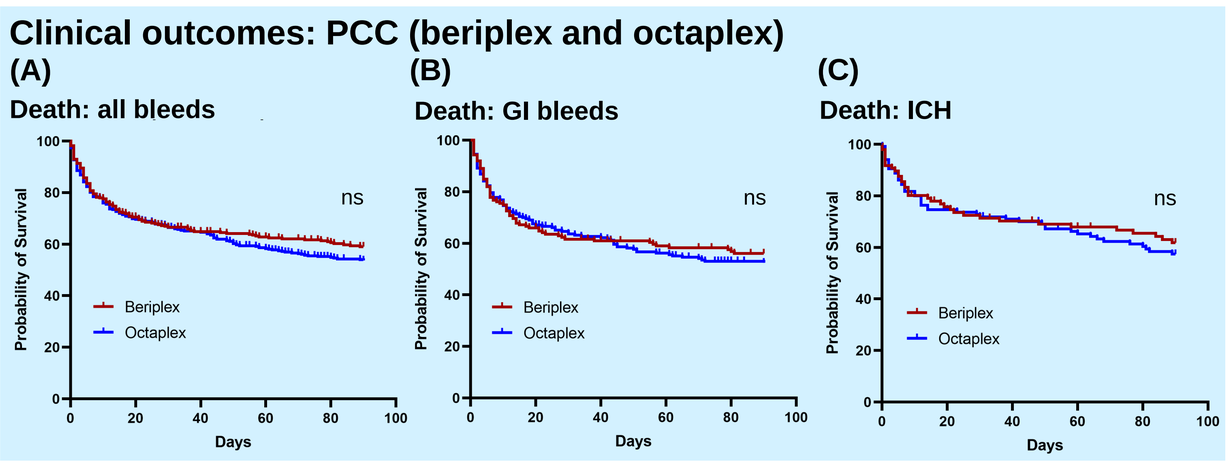

Figure 6. Clinical outcomes with PCC (beriplex and octaplex). Kaplan-Meier analyses (A) all bleeds, (B) GI bleeds, (C) ICH. Ns: not significant for difference by log rank test

Summary

- Large dataset of DOAC reversal with patient-level data
- 93% patients had major bleeding
- PCC dosing is heterogeneous and clinical outcomes are similar with beriplex and octaplex which are dosed differently
- 90 day mortality: 41%; 90 day incidence of thrombosis: 4%
- Median 4.3h from admission to reversal agent administration
- More data required on use of andexanet alfa and idarucizumab

Want to contribute?

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https://redcap.link/rapido

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