Clinical Consequences of Haematoma Expansion and Thrombotic Events in Patients With Factor Xa Inhibitor–associated ICH in ANNEXA-I

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Resource Information

About This Resource
These slides are one component of a continuing education program available online at MedEd On The Go titled What's New in Treating the Anticoagulated Patient with ICH?

Program Learning Objectives:
- Describe the various therapies necessary to manage the care of anticoagulated patients with ICH in the neurocritical care setting, including reversal and repletion
- Illustrate the latest neurosurgical clinical trial data to optimize care for patients with ICH
- Categorize the specific recommendations from the recent ESO guidelines on the management of ICH in the anticoagulated patient and describe approaches to implement them
- Outline the 3 elements of ICH care bundling and how each optimizes the care of the anticoagulated patient

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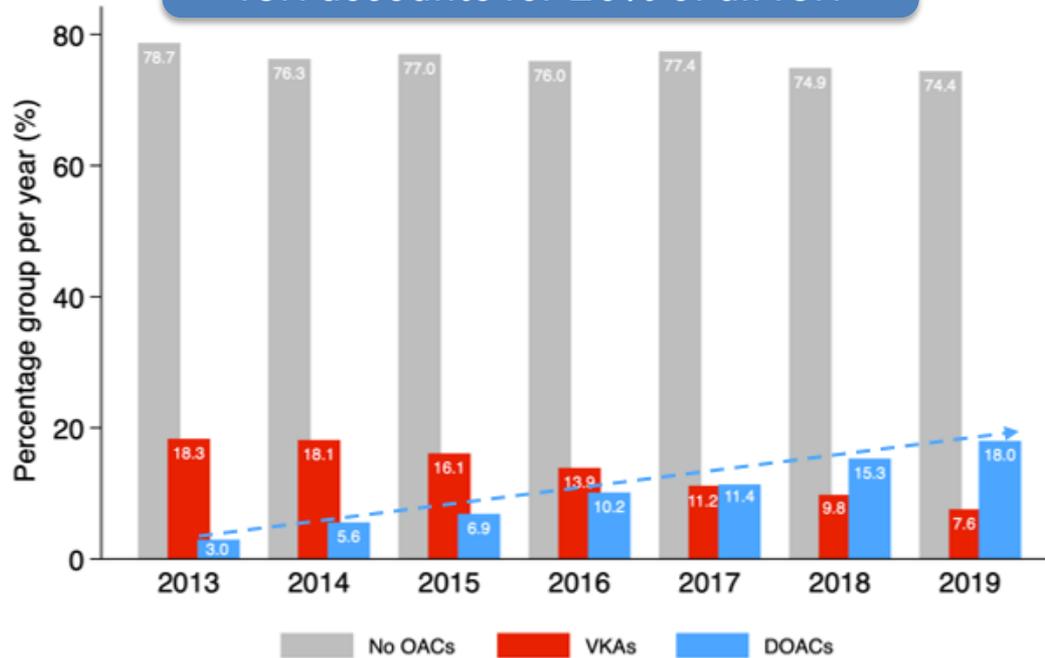
Disclosures

- This study and the secondary analyses were sponsored by Alexion, AstraZeneca Rare Disease

Background

Factor Xa inhibitor–associated ICH accounts for 20% of all ICH
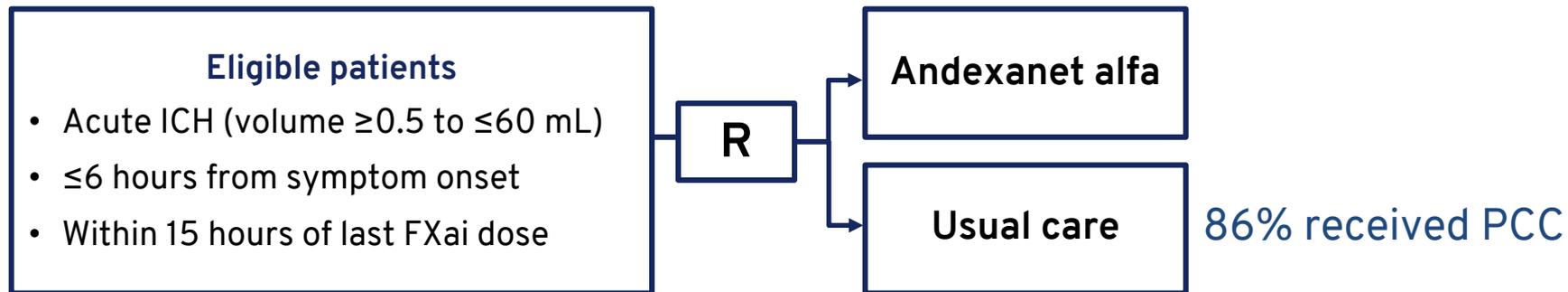
ANNEXA-I Design and Results

Eligible patients

- Acute ICH (volume ≥0.5 to ≤60 mL)
- ≤6 hours from symptom onset
- Within 15 hours of last FXai dose

R

Andexanet alfa

Usual care — 86% received PCC

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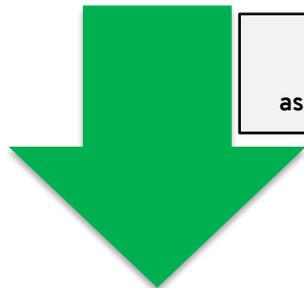**Andexanet alfa**

Usual care

86% received PCC
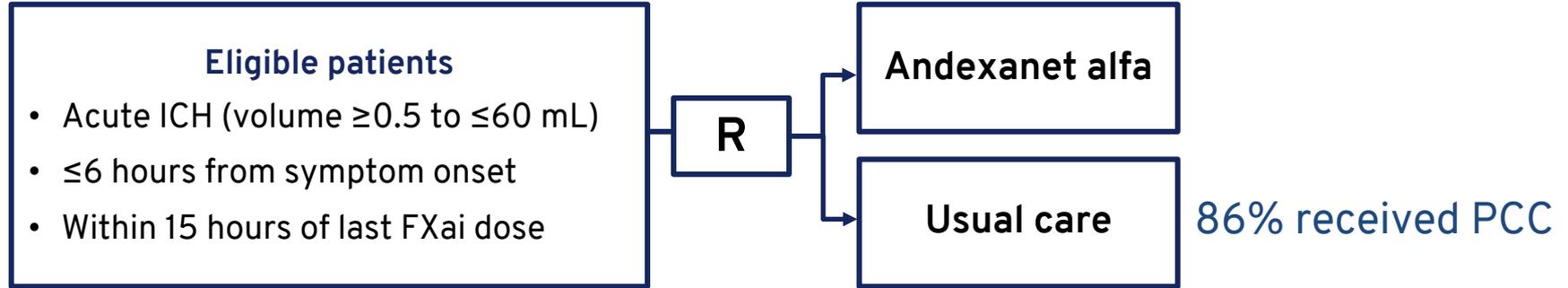
Treatment with andexanet alfa versus usual care

13.7%

Haematoma expansion*
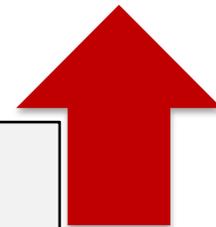
assessed in 459 patients with available baseline and follow-up scan

4.6%

Thrombotic events

assessed in all 530 patients enrolled

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Objective

To evaluate the clinical consequences of haematoma expansion and thrombotic events on all-cause mortality and functional outcomes to inform risk/benefit analyses

Time-dependent Cox regression model

- Outcome: **All-cause mortality* at Day 30**

- Main covariables of interest:

  - **Haematoma expansion** (defined as ≥12.5 mL or ≥35%)

  - **Thrombotic events** included as time-dependent covariates

- Further covariates: Age, female sex, prior myocardial infarction, prior stroke, prior congestive heart failure, pre-scan haematoma growth rate (mL/min)

*The most common causes of all-cause mortality were intracranial haemorrhage, pneumonia, respiratory failure.

5-day landmark analysis

- <u>Outcome</u>: **poor functional outcome (defined as modified Rankin Scale [mRS] scores of 4 to 6 at Day 30)**

- **Landmark analysis** starting at Day 5, including **all haematoma expansion and thrombotic events occurring up to Day 5**

- Logistic regression model adjusting for covariates

Mortality

Time-dependent Cox Regression Analysis for Mortality at Day 30

Variable	HR (95% CI)	*P* value
Thrombotic events	3.33 (1.73-6.42)	<0.001
Haematoma expansion	2.98 (2.00-4.43)	<0.001
Prior congestive heart failure	1.68 (1.05-2.67)	0.030
Pre-scan haematoma growth rate, mL/h	1.02 (1.01-1.03)	<0.001
Age, years	1.04 (1.01-1.07)	0.004
Female	0.70 (0.47-1.05)	0.087
Prior stroke	1.16 (0.74-1.83)	0.508
Prior myocardial infarction	1.16 (0.66-2.01)	0.607

Arterial Thrombotic Events and Mortality

Variable	HR (95% CI)	*P* value
Arterial thrombotic events	3.78 (1.95-7.32)	<0.001
Haematoma expansion	3.00 (2.01-4.46)	<0.001
Age, years	1.04 (1.01-1.07)	0.003
Female	0.69 (0.46-1.04)	0.078
Pre-scan hematoma growth rate (mL/hr)	1.02 (1.01-1.03)	<0.001
Prior stroke	1.15 (0.73-1.80)	0.556
Prior congestive heart failure	1.66 (1.04-2.65)	0.033
Prior myocardial infarction	1.15 (0.66-2.00)	0.624

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aOR (CI): 2.34 (1.49-3.68)

No. at risk:

Without HE	303	293	283	275	265	261
With HE	129	116	104	98	95	90

aOR, adjusted odds ratio; CI, confidence interval; HE, haematoma expansion.

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TE 5-day Landmark Analysis: 30-day Mortality

aOR (CI): 2.11 (0.74-6.00)

With TE

Without TE

No. at risk:
Without TE	419	396	375	363	351	342
With TE	13	13	12	10	9	9

aOR, adjusted odds ratio; CI, confidence interval; TE, thrombotic event.

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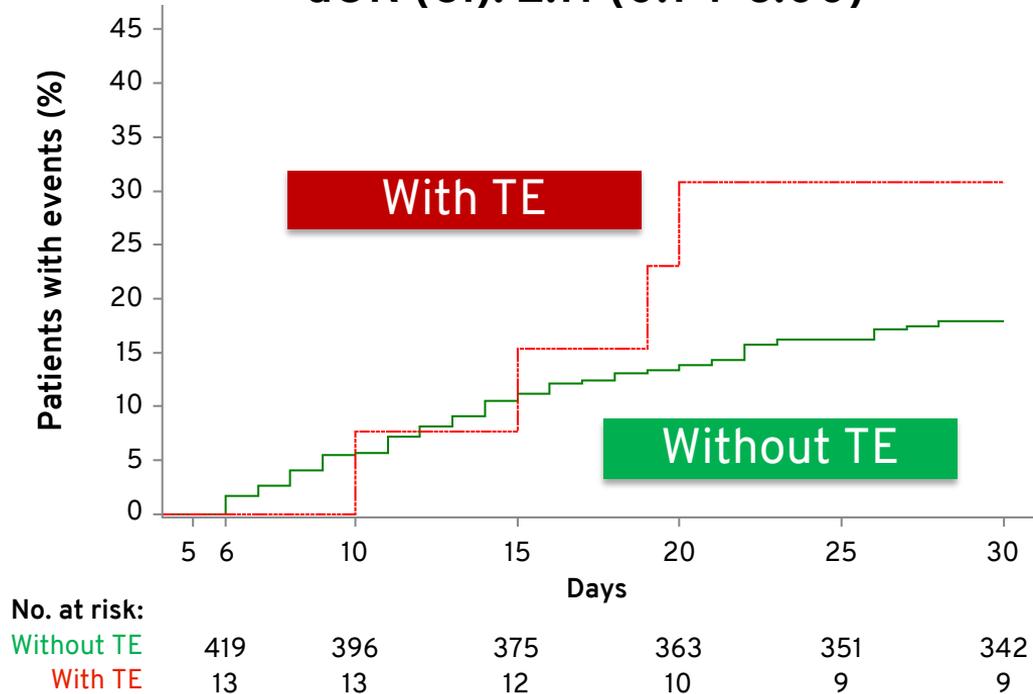
Poor
Functional Outcome

Landmark Analysis for mRS Scores of 4 to 6 at Day 30

Variable	OR (95% CI)	*P* value
Thrombotic events*	1.22 (0.33-4.45)	0.767
Haematoma expansion	1.93 (1.07-3.47)	0.029
Age, years	1.08 (1.05-1.12)	0.767
Female	0.62 (0.38-1.03)	0.068
Pre-scan haematoma growth rate, mL/h	1.26 (1.17-1.35)	<0.001
Prior stroke	1.18 (0.66-2.13)	0.577
Prior congestive heart failure	0.80 (0.41-1.56)	0.510
Prior myocardial infarction	0.69 (0.28-1.66)	0.402

Landmark Analysis: mRS Scores at Day 30

HE

Haematoma expansion

mRS 0–3: 39%

No (n = 293)	4 / 9 / 7 / 19 / 28 / 17 / 17
Yes (n = 141)	1 / 3 / 4 / 9 / 21 / 21 / 41

mRS 0–3: 17%

Percent (0 to 100)

TE

Thrombotic events

mRS 0–3: 32%

No (n = 394)	3 / 7 / 6 / 16 / 28 / 20 / 19
Yes (n = 13)	31 / 8 / 31 / 31

mRS 0–3: 31%

Percent (0 to 100)

mRS score: 0 · 1 · 2 · 3 · 4 · 5 · 6
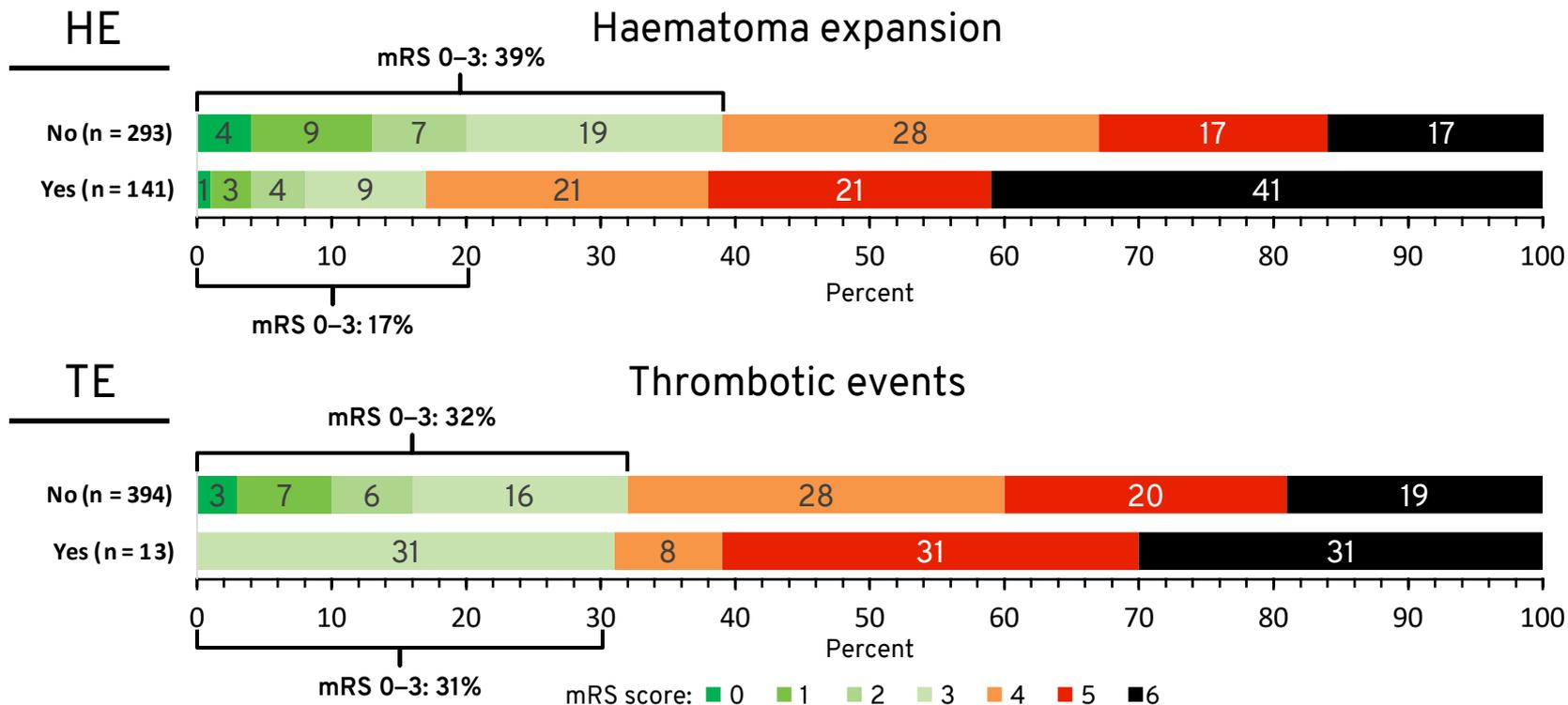
Limitations

- Post-hoc analysis

- Due to low event rates, firm conclusions cannot be drawn regarding the association between thrombotic events and mRS scores of 4 to 6

- Functional outcome assessment at 30 days is early for patients with ICH

Summary and Conclusions

- Both haematoma expansion and thrombotic events were strongly associated with death at Day 30

- Haematoma expansion was associated with poor functional outcome (mRS scores of 4 to 6)

- Haematoma expansion was 4x more frequent than thrombotic events

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