PRAGUE-26

(Design & Rationale)

A Multicentre, Randomized Trial of Catheter-Directed Thrombolysis in Intermediate-high Risk Acute Pulmonary Embolism

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On behalf of PRAGUE-26 investigators

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A Pilot randomised trial of Catheter-directed Thrombolysis

A pilot randomised trial of catheter-directed thrombolysis or standard anticoagulation for patients with intermediate-high risk acute pulmonary embolism

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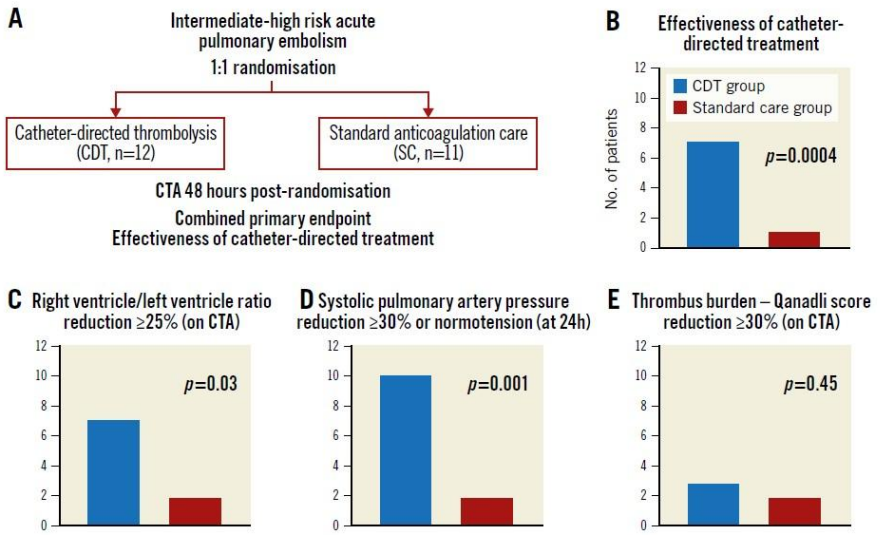
CENTRAL **ILLUSTRATION** Combined primary endpoint effectiveness of catheter-directed thrombolysis.



A) Study design. B) Combined primary endpoint effectiveness of catheter-directed treatment – at least two of three predefined criteria – per C), D), E) had to be met. CDT: catheter-directed thrombolysis; CTA: computed tomography angiography; SC: standard care

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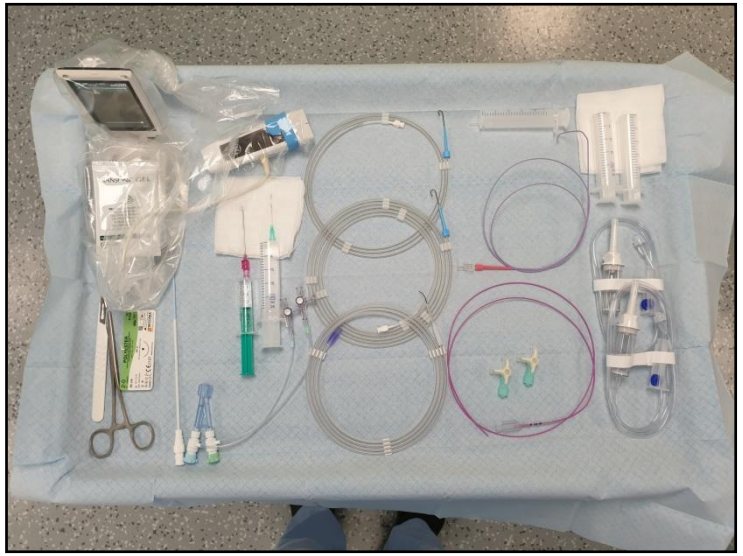
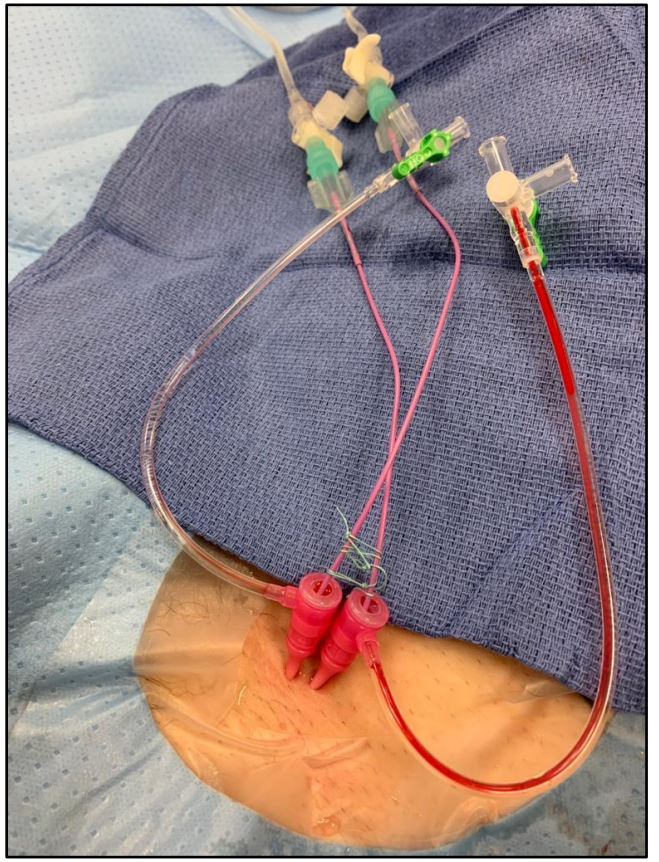
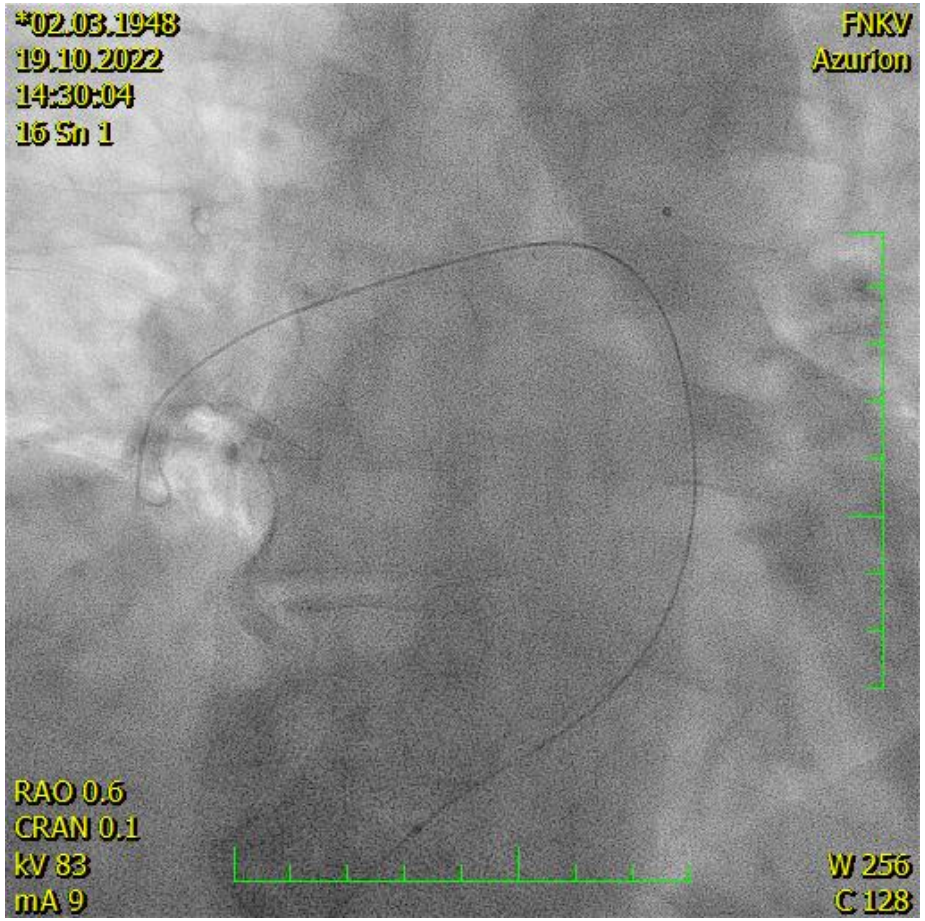
Local Thrombolysis (4F)

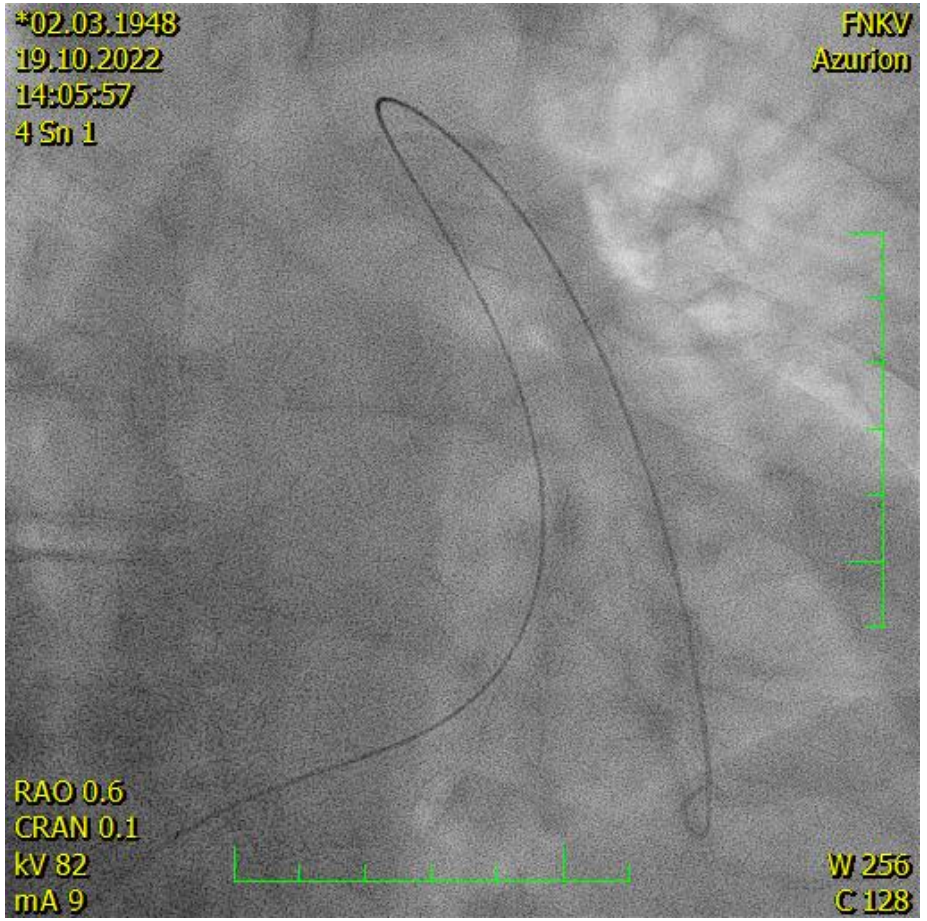
- Simple = Available = Cheap
- Minimally invasive (2x 4F ev. 1x 8F)
- Reduced dose of tPA (20mg)
- No contrast needed



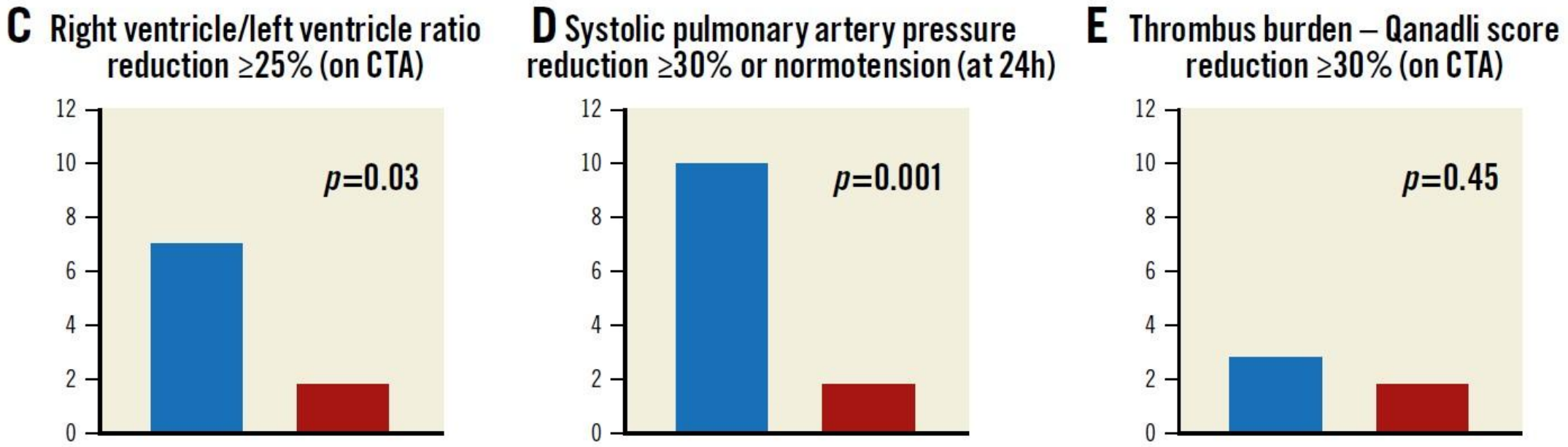


Catheter placement (4F)





Pilot study – results (primary endpoint)



- RV/LV ratio reduction ≥25% on CTA (7 ze 12 vs. 2 z 11 *in favor of CDT*)
- sPAP reduction ≥30% or normotension at 24h (10 ze 12 vs. 2 z 11 *in favor of CDT*)
- Thrombus burden – Qanadli score reduction ≥30% on CTA (3 ze 12 vs. 2 z 11, no difference)

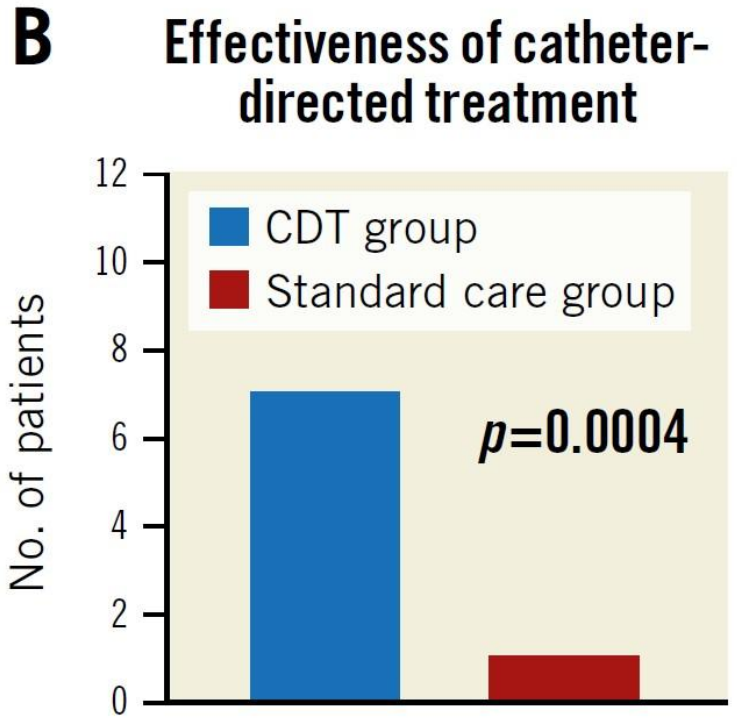
Pilot study – results (primary endpoint)

Efectiveness of Catheter-directed Treatment

- 7 of 12 in the CDT group vs. 1 z 11 in Standard care group *(p=0.0004)*

Safety of Catheter-directed Treatment

- No intracranial of life-threatening bleeding



PRAGUE-26
(Viktor Kočka, Josef Kroupa et al.)

- **Non-industry sponsored**
- 558 patients

- Aim = evaluate clinical outcomes in patients with intermediate-high risk acute pulmonary embolism, comparing catheter-directed thrombolysis (CDT) to standard anticoagulation therapy

- 11 active Interventional centres in Czech Republic

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TRIAL DESIGN

Design and rationale of PRAGUE-26: a multicentre, randomised trial of catheter-directed thrombolysis for intermediate-high risk acute pulmonary embolism

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PRAGUE-26

(Design, Inclusion & Exclusion criteria)

- Prospective
- Multicentric
- Randomised
- Active-controlled
- Unblinded
- Parallel-group

- Phase IV, Interventional study

Table 2. Inclusion and Exclusion Criteria	
Inclusion criteria	1. Age > 18 years and ≤ 80 years.
	2. Computed tomography angiography (CTA)-verified proximal* PE AND symptom onset < 14 days prior.
	3. Intermediate-high risk PE with a SPESI score ≥ 1 AND RV dysfunction** AND an elevated biomarker *** (hs-troponin or NT-proBNP) level.
	4. Signed informed consent.
Exclusion criteria	1. Active clinically significant bleeding.
	2. Any haemorrhagic stroke OR a recent (< 6 months) ischaemic stroke/transient ischaemic attack.
	3. Recent (< 3 months) cranial trauma OR another active intracranial/intraspinal process.
	4. Major surgery within 7 days prior.
	5. Active malignancy OR other severe illness with expected survival < 2 years.
	6. Haemoglobin level < 80 g/L; international normalised ratio > 2.0, platelet count ≤ 100 x 10^9; creatinine level > 200 µmol/L.
	7. Pregnant or breastfeeding, fertility without previous exclusion of gravidity.
	8. Allergic to thrombolytics or heparin or low-molecular-weight heparin (LMWH), contrast allergy, a history of heparin-induced thrombocytopenia.
	9. Floating thrombi in transit through a patent foramen ovale.
	10. Participation in another clinical trial.

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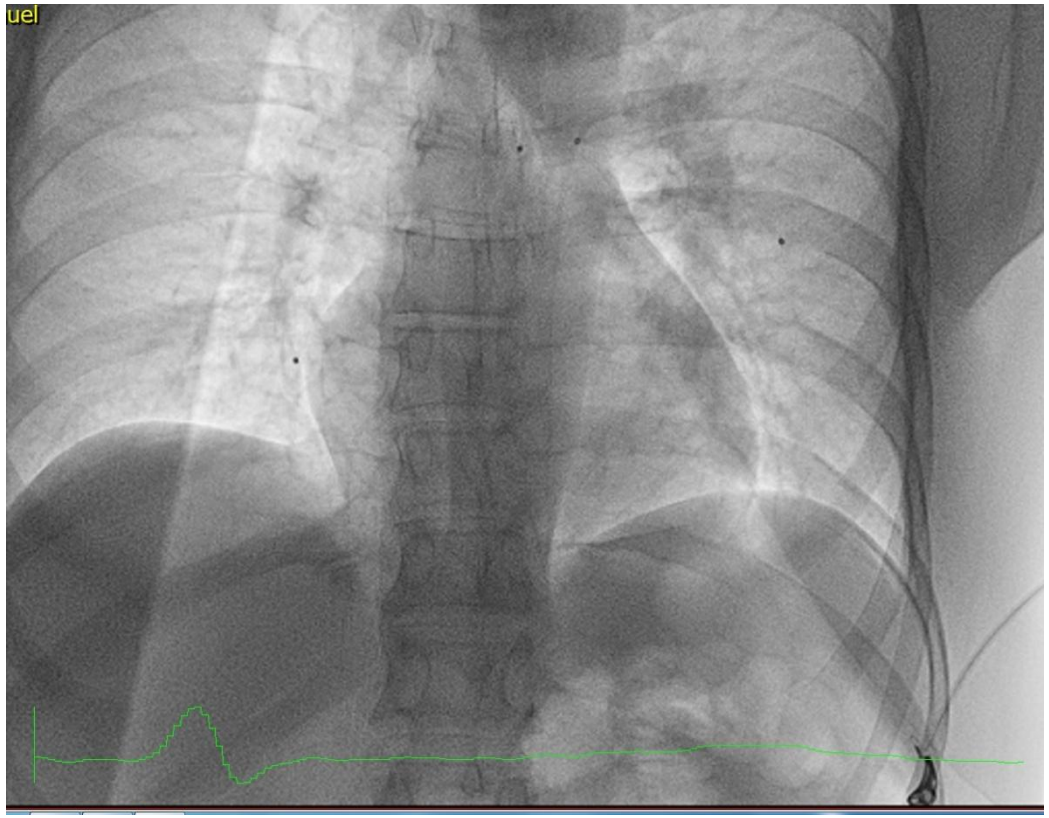
(Design, Intervention)

- Alteplase (tPA)
- Bolus: 1mg/catheter (cath-lab)
- With subsequent Alteplase infusion 1 mg/h/catheter for 9 hours
- Total dose 20 mg of Alteplase in bilateral acute PE (10 mg in unilateral PE)



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(Design, primary endpoint)

- „**HARD**“ primary endpoint, clinical composite:

- **All-cause mortality**
- **PE recurrence**
- **Cardiorespiratory decompensation / collapse**

- Within 7 days of randomization

4.1 Primary endpoint – combined; clinical composite of any of the following parameters

1) **All-cause mortality** – [Time Frame: Within 7 days of randomization]
2) **PE recurrence** (non-fatal symptomatic and objectively confirmed recurrence of PE by repeated CTA) – [Time Frame: Within 7 days of randomization]
3) **Cardiorespiratory decompensation or collapse*** – [Time Frame: Within 7 days of randomization]

** Defined as at least one of following criteria:*

a) cardiac arrest or need for CPR at any time between randomization and day 7;

b) signs of shock: new-onset of persistent arterial hypotension (systolic blood pressure below 90 mmHg or systolic blood pressure drop by at least of 40 mmHg, over at least 15 minutes and despite an adequate volume status; or need for vasopressors to maintain systolic blood pressure of at least 90 mmHg), accompanied by end-organ hypoperfusion (altered mental status; oliguria/anuria; or increased serum lactate >2 mmol/L) at any time between randomization and day 7;

c) placement on extracorporeal membrane oxygenation (ECMO);

d) intubation, or initiation of non-invasive mechanical ventilation at any time between randomization and day 7;

e) National Early Warning Score (NEWS) of 9 or higher, between 24 hours and 7 days after randomization, confirmed on consecutive measurements taken twice, 15 minutes apart.

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(Design, secondary endpoints)

- Bleeding complications
- First-line therapy failure
- ICU/ total lenght of stay
- Functional outcomes, QoL assessment
- Economical aspects etc.

4.2 Secondary endpoints

1. All individual components of primary endpoint – [Time Frame: Within 7 days, 30 days, and 12 months]
2. First-line therapy failure** – [Time Frame: Hospitalization]

*** Defined as administration of systemic thrombolysis during first (index) hospitalization for acute PE.*

3. Ischemic or haemorrhagic stroke [Time Frame: Within 7 days and 30 days]
4. Serious adverse events – [Time Frame: Within 12 months]
5. Duration of hospitalization for the index acute PE event (Time from admission to discharge from hospital) – [Time Frame: Within 30 days]
6. Duration of stay at the intensive, intermediate or coronary care unit during hospitalization for the index acute PE event (Time from admission to discharge from ICU, intermediate, or CCU) – [Time Frame: Within 30 days]
7. Hospitalization cost (cost-effectiveness analysis) – [Time Frame: Within 30 days]
8. GUSTO major (moderate and severe) bleeding*** – [Time Frame: Within 30 days]

*** Major bleeding will be adjudicated according to the GUSTO criteria:*

GUSTO severe or life-threatening bleeding: A bleeding episode that leads to hemodynamic compromise requiring emergency intervention (such as replacement of fluid and/or blood products, inotropic support, or surgical treatment), or is life-threatening or fatal.

GUSTO moderate bleeding (a bleeding episode requiring blood transfusion(s), but which is not deemed life-threatening and does not lead to hemodynamic compromise requiring emergency fluid replacement, inotropic support, or interventional treatment).

9. International Society on Thrombosis and Hemostasis (ISTH) major bleeding**** – [Time Frame: Within 30 days]

**** Major bleeding will be adjudicated according to the ISTH criteria:*

Fatal bleeding and/or

Symptomatic bleeding in a critical area or organ (intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome) and/or

Bleeding causing a fall in hemoglobin level of 20 g/L (2 g/dL) or more, or leading to transfusion of two or more units of whole blood or red blood cells.

10. All bleeding complications scored by the Bleeding Academic Research Consortium (BARC) classification – [Time Frame: Within 30 days and 12 months]
11. Change in the RV-to-LV diameter ratio, systolic pulmonary artery pressure (sPAP), Tricuspid annular plane systolic excursion (TAPSE), Tissue Doppler imaging-derived Tricuspid lateral annular Systolic Velocity (S´ TDI) as measured by echocardiography – [Time Frame: Between Randomization and 24±3 hours, at 30 days, 12 months and 24 months]

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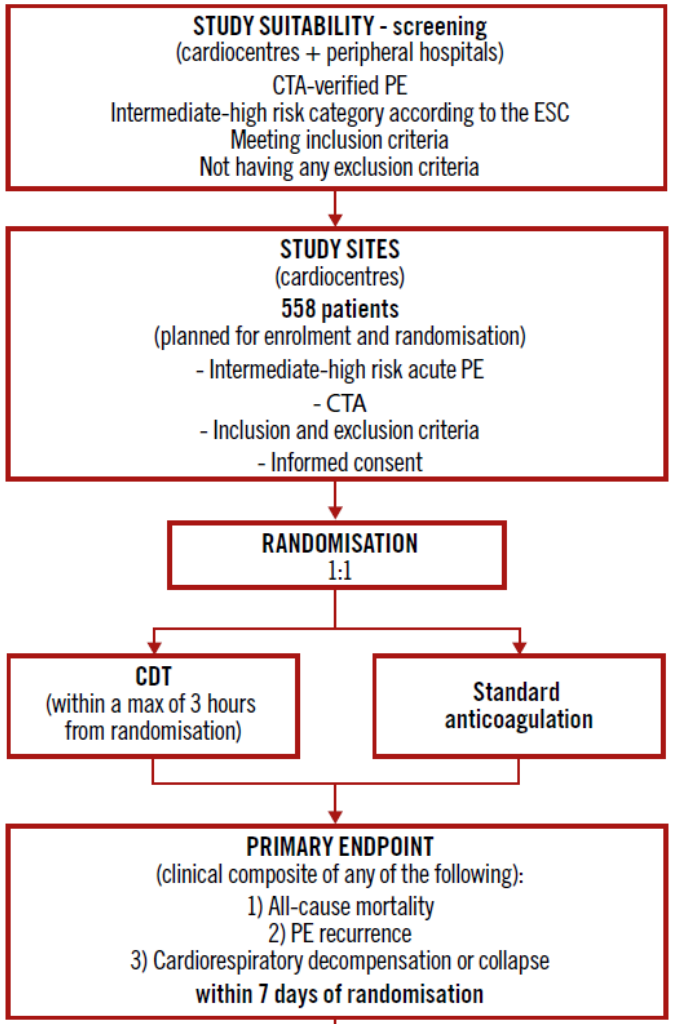
(Study flow diagram)



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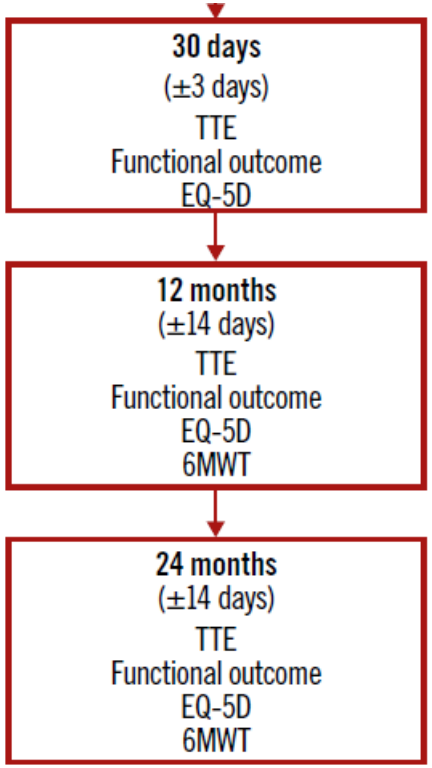
(Study flow diagram)



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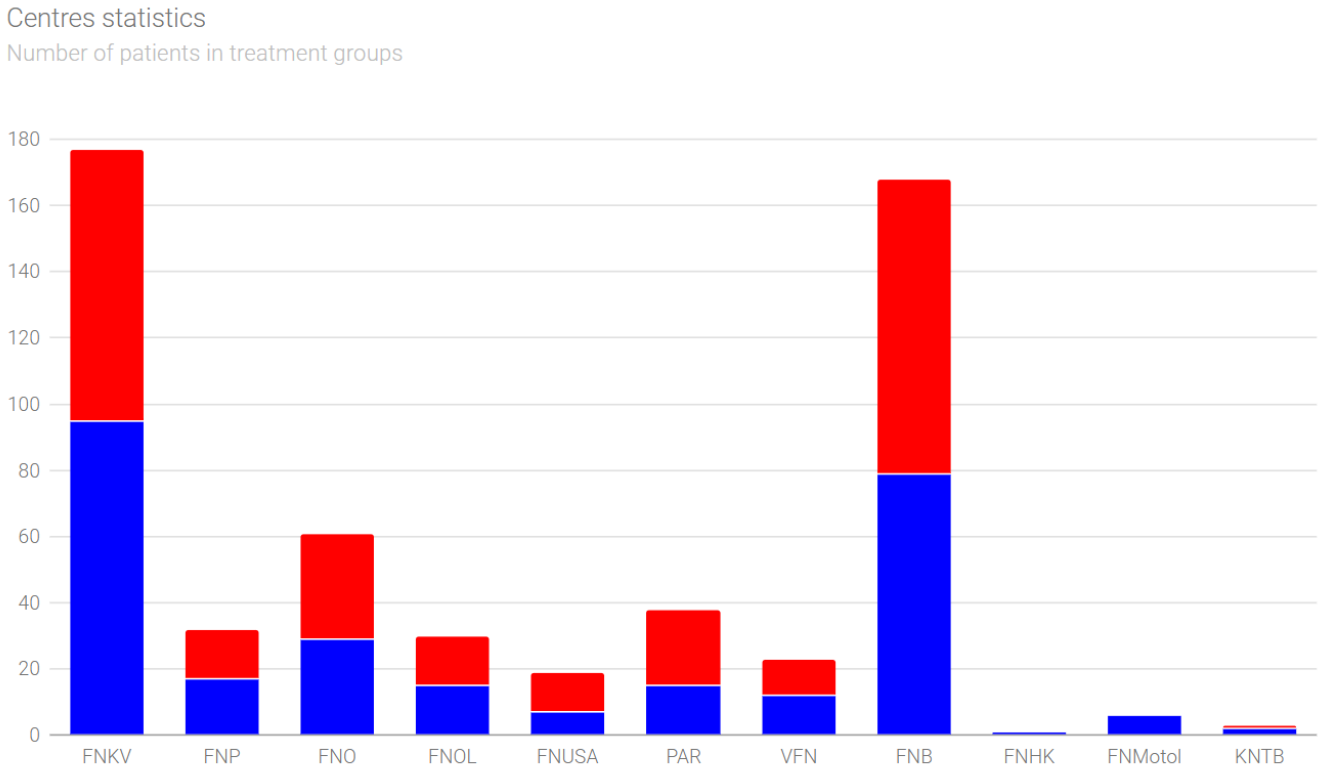
(Enrolment completed)

- 558 subjects randomised
- 11 active centres across Czechia
- **End of enrolment 23-Mar-2026**
- **Results publication 3Q/2026** (estimated)



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(Questions to be Answered)

- **… whether a simple, low-cost Catheter-directed Thrombolysis is superior to standard anticoagulation alone in intermediate-high risk acute PE (as defined by ESC Guidelines)?**

- … and many more (bleeding complications?, cost-effectiveness?, functional outcomes? etc.)

- Many thanks to all of the patients, healthcare staff and all Prague-26 investigators!
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25-26/SEP/2026

PE Intervention Academy

SAVE THE DATE

25–26 September 2026
Prague, Czech Republic

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