Supplementary Online Content

Gladstone DJ, Aviv RI, Demchuk AM, et al; SPOTLIGHT and STOP-IT Investigators and Coordinators. Effect of recombinant activated coagulation factor VII on hemorrhage expansion among patients with spot sign–positive acute intracerebral hemorrhage: the SPOTLIGHT and STOP-IT randomized clinical trials. *JAMA Neurol*. Published online August 19, 2019. doi:10.1001/jamaneurol.2019.2636

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. List of participating sites, investigators, and coordinators

Executive Committee: David J. Gladstone MD, Matthew L. Flaherty MD, Andrew M. Demchuk MD, Michael D. Hill MD, Richard I. Aviv MBChB

Biostatisticians: Kevin Thorpe PhD, Jane Khoury PhD, Heidi Sucharew PhD

Project Managers/Research Coordinators/Study Monitors: Judith Hall, Stephanie De Masi, Val Panzov, Natascha Kozlowski, Amr Sharaf, Janice Carrozzella

Spot Sign Training Module: Richard I. Aviv MBChB, Thien Huynh MD, University of Toronto, Canada

SPOTLIGHT Study

DSMB: Gordon Gubitz MD, David Anderson MD, Michael Love MD, George Wells PhD

Bioethicists: Julie Spence MD, Michel Shamy MD

Participating Sites, Site Investigators and Coordinators

Sunnybrook Health Sciences Centre, Toronto: Richard H. Swartz MD (site PI), David J. Gladstone MD, Karl Boyle MDCoordinators: Maria Braganza, Nadia Fedasko, Dolores Golob, Edith Bardi, Samantha Senyshyn, Megan Cayley, Connie Colavecchia

Foothills Medical Centre, Calgary: Andrew M. Demchuk MD (site PI), Michael D. Hill MD, Shelagh Coutts MD, Gary Klein MD, Bijoy Menon MD, Tim Watson MD, Eric Smith MD, Suresh Subramaniam MD, Simerpreet Bal MD, Philip Barber MD, Marie-Christine Camden MD, Myles Horton MD, Sachin Mishra MD, Vivek Nambiar MD, Andres Venegas Torres MD, Sweta Adatia MD, Amjad Alseraya MD, Jamsheed Desai MD, Jennifer Mandzia MD, Michel Shamy MD, Anurag Trivedi MD, Philip Choi MD, Veronique Dubuc MD, Evgenia Klourfeld MD, Thalia Field MD, Dilip Singh MD, Tapuwa Musuka MD, Sarah Bloujney MD, Davar Nikneshan MD, Oje Imoukhuede MD, Amy Yu MD, Ramana Appireddy MD, Jamie Evans MD.
Coordinators: Karla Ryckborst, Carly Calvert

The Ottawa Hospital, Ottawa: Dariush Dowlatshahi MD (site PI), Grant Stotts MD, Mukul Sharma MD
Coordinators: Sohail Robert, Melodie Mortensen, Rany Shamloul

Toronto Western Hospital, Toronto: Martin Del Campo MD (site PI), Frank L. Silver MD, Leanne Casaubon MD, Cheryl Jaigobin MD, Yael Perez MD
Coordinators: Libby Kalman, Jemini Abraham, Relu Wiegner, Anne Cayley, Victoria Riediger

Walter C. Mackenzie Health Sciences Centre, Edmonton: Ken Butcher MD (site PI), Mahesh Kate MD, Thomas Jeerakathil MD, Ashfaq Shuaib MD
Coordinators: Sylvia Gaucher, Leka Sivakumar

Vancouver General Hospital, Vancouver: Samuel Yip MD (site PI), Philip Teal MD, Andrew Woolfenden MD, Oscar Benavente MD, Jeff Beckman MD, Colleen Murphy MD, Thalia Field MD, Negar Asdaghi MD
Coordinator: Karina Villaluna-Murray

Hamilton Health Sciences, Hamilton: Demetrios J. Sahlas MD (site PI), Almunder Algird MD
Coordinators: Jordan Knapman, Sue Macmillan, Janice Sancan

Trillium Health Partners, Mississauga: Manu Mehdiratta MD (site PI), Yael Perez MD, Verity John MD, Al-Noor Dhanani MD, Bryan Temple MD, Andre Douen MD
Coordinator: Suzanne Bickford

St. Michael's Hospital, Toronto: Daniel Selchen MD (site PI), Gustavo Saposnik MD
Coordinator: Pawel Kostyrko

London Health Sciences Centre, London: Richard Chan MD (site PI), Bryan Young MD, Balagopal Kumar MD, Peter Soros MD,
Coordinators: Kimberley Hesser, Mary Wright, Connie Frank, Belinda Amato-Marziali

Hopital Notre-Dame, Montreal: Yan Deschaintre MD (site PI), Alexandre Poppe
Coordinator: Marlene Lapierre

Hopital Charles Le Moyne, Greenfield Park: Jean-Martin Boulanger MD (site PI), Leo Berger MD
Coordinator: Lise Blais, Christel Simard

Montreal Neurological Institute, Montreal: Jeanne Teitelbaum MD (site PI)
Coordinator: Natasha Campbell

Kingston General Hospital, Kingston: Al Jin MD (site PI)
Coordinator: Adriana Breen

STOP-IT Study

External Medical Safety Monitors: Claude Hemphill MD, University of California, San Francisco; David Gregg MD, Medical University of South Carolina

Participating Sites (that enrolled 1 or more patients), Site Principal Investigators and Coordinators

Massachusetts General Hospital: Joshua Goldstein MD
Coordinators: Laura Meloney, Ryan T. Callahan, Kristen McNamara, Lauren Barton

Medical University of South Carolina: Edward Jauch MD
Coordinators: Bobby Navarro, Gina Keller

St. Joseph's Medical Center: James Frey MD
Coordinator: Jean Lopez

Sunnybrook Health Science Centre, Toronto, Canada: David J. Gladstone MD
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Foothills Medical Centre, Calgary, Canada: Andrew M. Demchuk MD
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University of Cincinnati: Matthew Flaherty MD
Coordinators: Traci Doellman Zorn, Alisha Hodge, Mary Haverbusch, Jane Eilerman

University of Pennsylvania: Brett L. Cucchiara MD
Coordinators: Mary Liz DeSanto, Melissa Kruszewski

University of Pittsburgh Medical Center: Maxim D. Hammer MD
Coordinators: Jill Oakley, Angela Adams, Kara Armbruster

University of Texas Southwestern: Christina Hall MD
Coordinators: Claudette Lohr, Jan Cameron-Watts

University of California San Diego: Thomas Hemmen MD
Coordinators: Teresa Rzesiewicz, Ronelyn Chavez

Washington University: Peter Panagos MD
Coordinators: Jill Newgent, James Franke, Rachael Sargent

eTable 1. Main trial inclusion and exclusion criteria

	STOP-IT	SPOTLIGHT
Inclusion Criteria		
Age, years	18-80	18-85; upper age limit later removed
Time window for enrolment	Onset to CT ≤ 5 hours	Able to be treated within 6 hours from onset
Target time from baseline CT to study drug administration	≤ 90 minutes	≤ 60 minutes
Exclusion criteria		
ICH Location	Brainstem ICH	Brainstem and cerebellar ICH
Antithrombotic agents	Vitamin K antagonist with INR >1.2, unfractionated heparin with abnormal PTT; LMWH; DTI; Xa inhibitor; GPIIb/IIIa antagonist	Vitamin K antagonist with INR >1.4, unfractionated heparin with abnormal PTT, LMWH; DTI; Xa inhibitor; GPIIb/IIIa antagonist
Baseline ICH volume	< 0·5 ml or > 90·0 ml	< 3·0 ml or > 70·0 ml (upper limit later increased to 90·0 ml)
Baseline Glasgow Coma Scale score	<8	<8 (this exclusion was later removed)
Baseline laboratory testing	Abnormal baseline troponin, INR > 1.2, platelets <50,000/μl, creatinine >1.4 mg/dL for sites not performing CT angiography as standard of care	Abnormal baseline troponin (later removed), INR >1.4, platelets <50,000/ μl
Thromboembolism	Any prior thromboembolism	Any thromboembolism within 6 months
Pre-existing disability	Modified Rankin Scale score >2	Modified Rankin Scale score >2; (this disability exclusion was later removed)

For a complete listing of all eligibility criteria see the study protocols.
CT = computed tomography; ICH = intracerebral hemorrhage; LMWH = low molecular weight heparin; DTI = direct thrombin inhibitor

eTable 2. Coefficient and effect estimates from adjusted models

	Log Volume		Percentage Change in Volume		
	β	SE	Effect	95% CI	P-value
Primary model					
Treatment group (rFVIIa versus placebo)	-0.018	0.12	1.8% reduction	27% reduction to 23% increase	0.9
Log baseline ICH volume (per 20% increase)	0.19	0.016	19% increase	16% increase to 22% increase	<0.0001
Stroke onset to study drug administration (per 30 minute increase)	-0.032	0.12	3.2% reduction	8.9% reduction to 2.4% increase	0.3
Secondary model					
Treatment group (rFVIIa versus placebo)	-0.015	0.13	1.5% reduction	27% reduction to 24% increase	0.9
Log baseline total intracranial hemorrhage volume (ICH plus IVH) (per 20% increase)	0.17	0.017	17% increase	13% increase to 20% increase	<0.0001
Stroke onset to study drug administration (per 30 minute increase)	-0.033	0.030	3.2% reduction	9,1% reduction to 2.6% increase	0.3

The coefficients and standard errors are obtained from the linear regression model with log-volume as the outcome. The effects and 95% confidence intervals re-express the coefficients in terms of percentage differences in the response on original units.

eTable 3. Ischemic adverse events within the first 4 days after randomization

Adverse event	rFVIIa group (n = 32)	Placebo group (n = 37)	p-value
Myocardial infarction, ischemic stroke, or pulmonary embolism	2 (6.3%)	4 (10.8%)	0.68
ST elevation myocardial infarction	0	0	1.00
Non-ST elevation myocardial ischemia or infarction†	1 (3.1%)	3 (8.1%)	0.62
Isolated troponin elevation above local laboratory upper limit of normal reference range, without clinical or ECG changes of myocardial ischemia	9 (28.1%)	10 (27.0%)	1.00
Ischemic stroke within 4 days	1** (3.1%)	1* (2.7%)	1.00
Pulmonary embolism	0	0	1.00
Deep vein thrombosis	0	0	1.00
Other thromboembolic event	1^ (3.1%)	1$ (2.7%)	1.00

Data are n (%).

†Troponin elevation was defined as levels >0·1 mcg/L to account variations in troponin laboratory testing protocols between sites. For example, some hospitals used high sensitivity troponin T testing and others used routine troponin T or troponin I testing.

*Acute cerebral infarct diagnosed post-operatively following hemicraniectomy for hematoma evacuation.

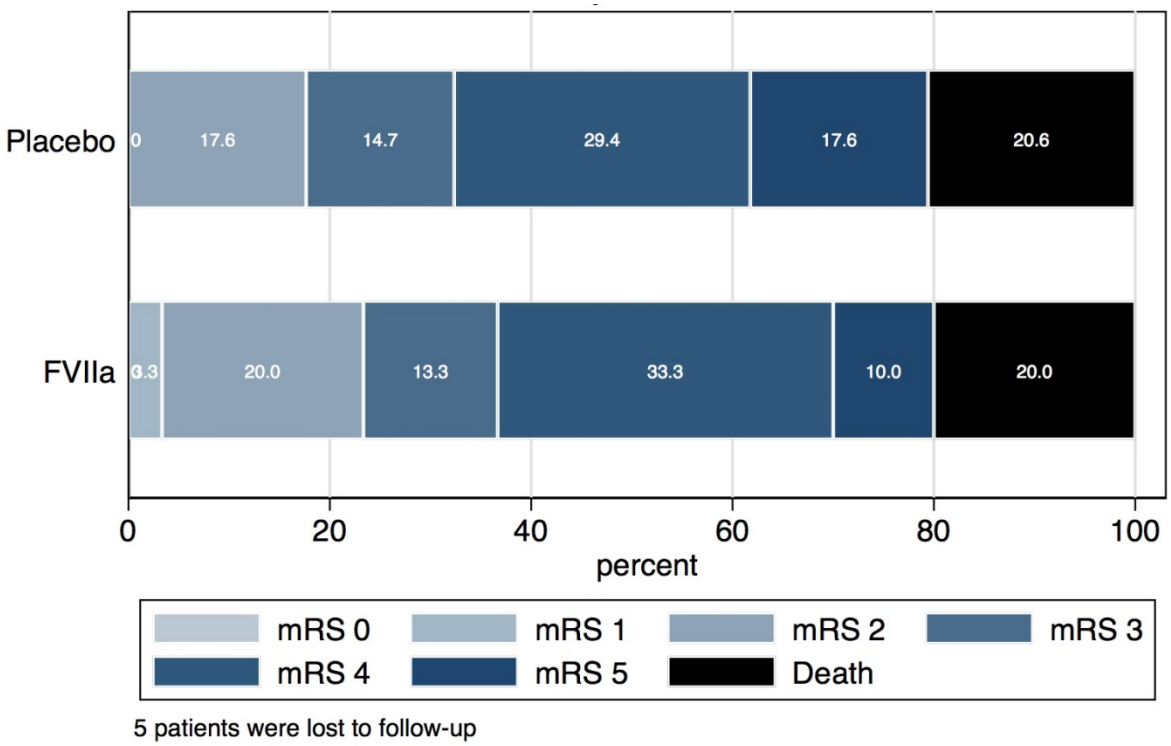
**Incidental asymptomatic MRI-detected tiny acute cerebral infarct, adjacent to large index ICH.

^ One patient had an imaging diagnosis of possible middle cerebral artery thrombosis on MR angiography that was asymptomatic and without evidence of infarction on brain MRI (DWI negative).

$ Superficial vein thrombosis (upper limb)

P-values for the between-group comparisons from Fisher's Exact test.

eFigure. 90-Day modified Rankin Scale scores



5 patients were lost to follow-up