

Bleeding complications in patients loaded with ticagrelor or DOACS – What can we do?

Nandor Marczin, MD, PhD



Imperial College London



Royal Brompton Harefield Hospitals



70TH ESCVS, 2022”



70th ESCVS

Satellite Symposium

June 22nd, 2022
12:30 - 13:30 pm CET
Liège, Belgium

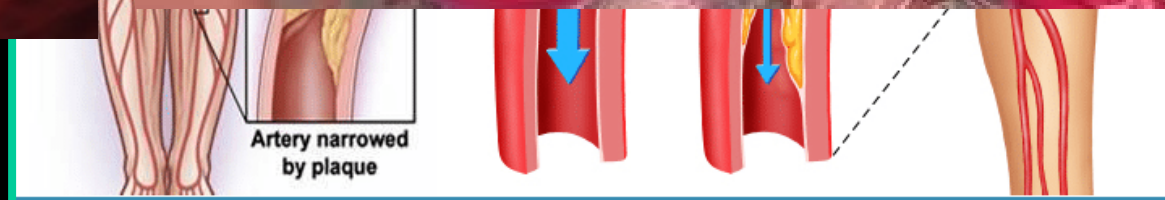
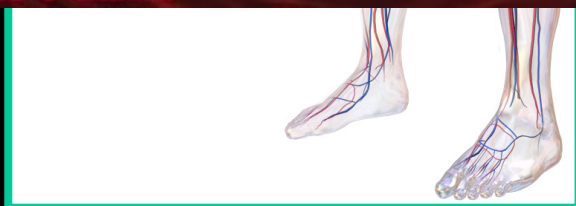
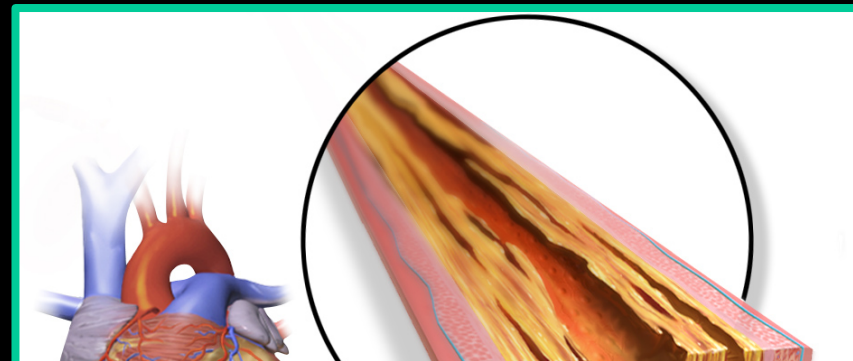
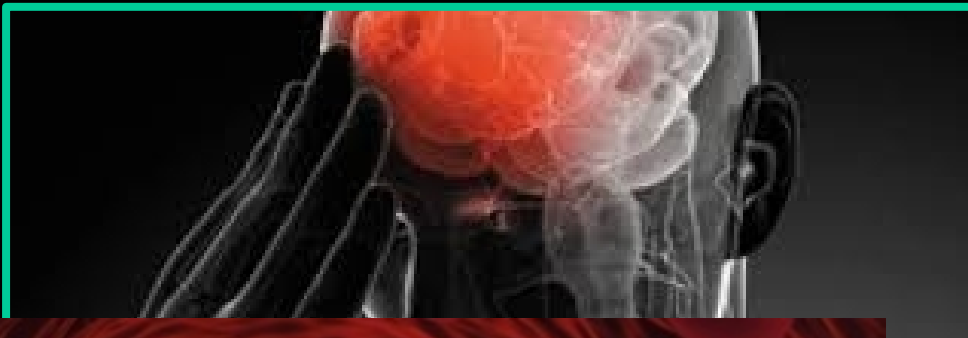
CytoSorbents™
WORKING TO SAVE LIVES

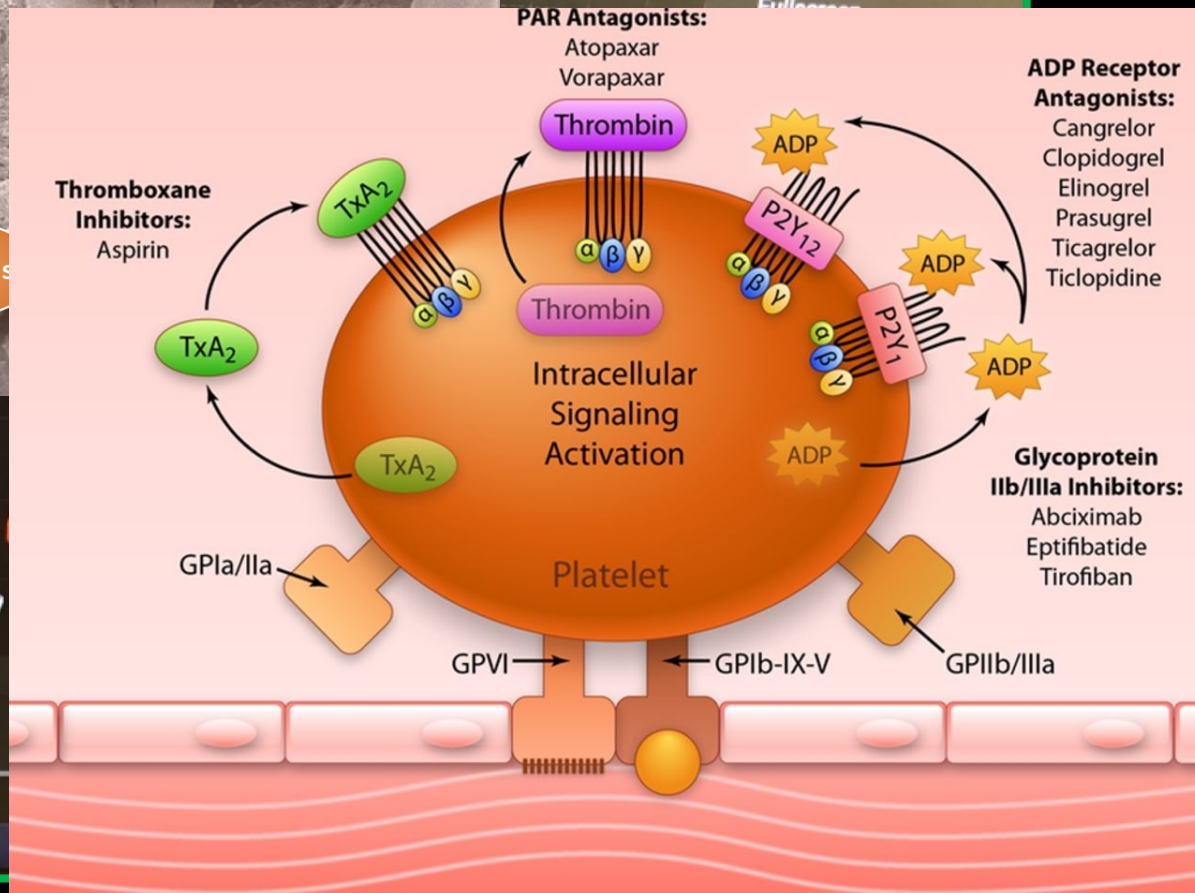
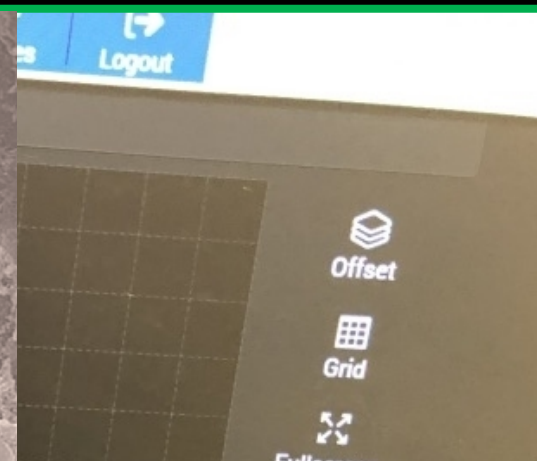
LIEGE, BELGIUM

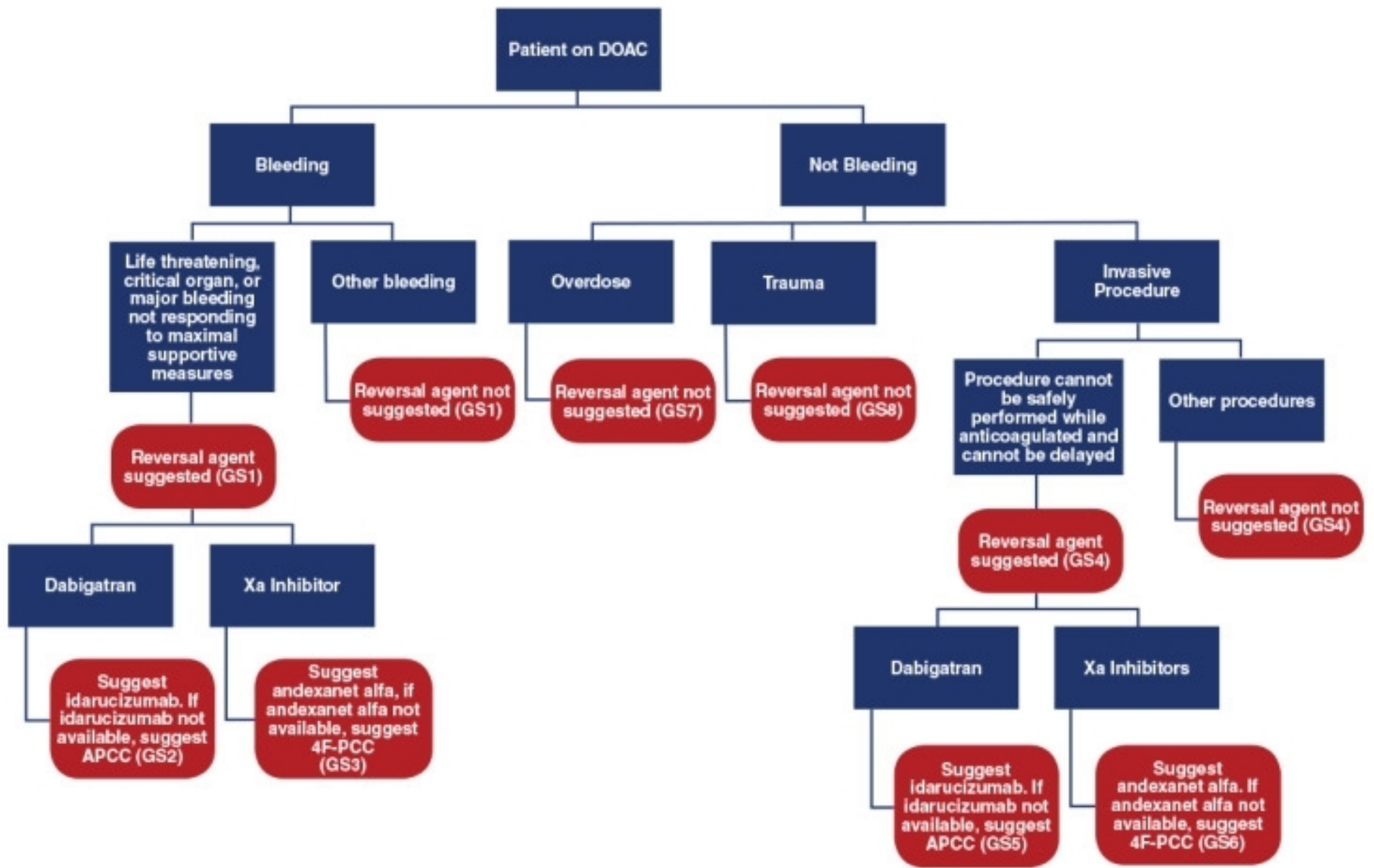
Conflict of Interest



- ❖ Conference, advisory board travel attendance
- ❖ Lecture fees
- ❖ Research grant
- ❖ Study PI
- ❖ NICE external commentator







Anticoagulants and antiplatelets: Cardiology dream ⇔ Perioperative nightmare

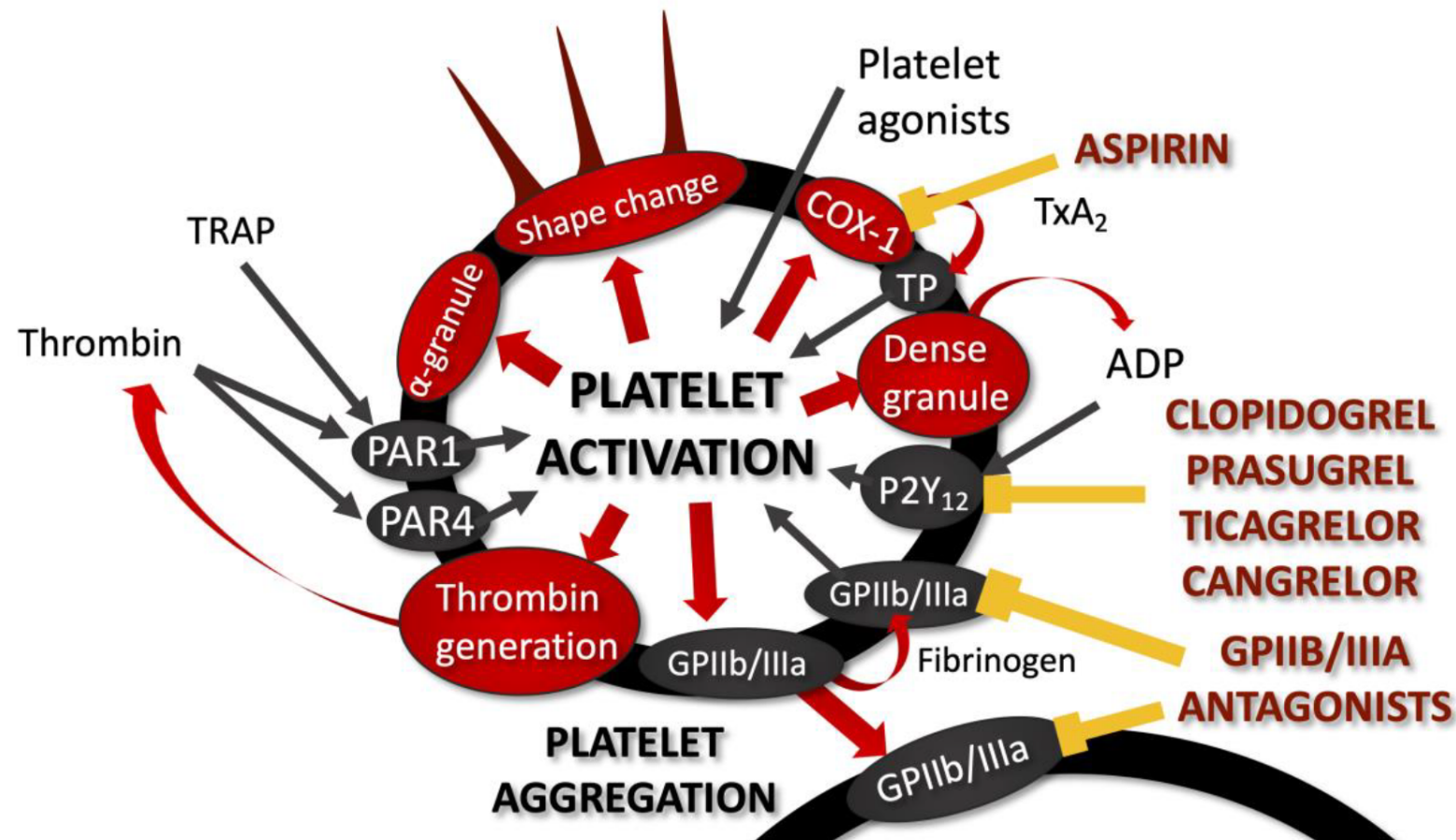


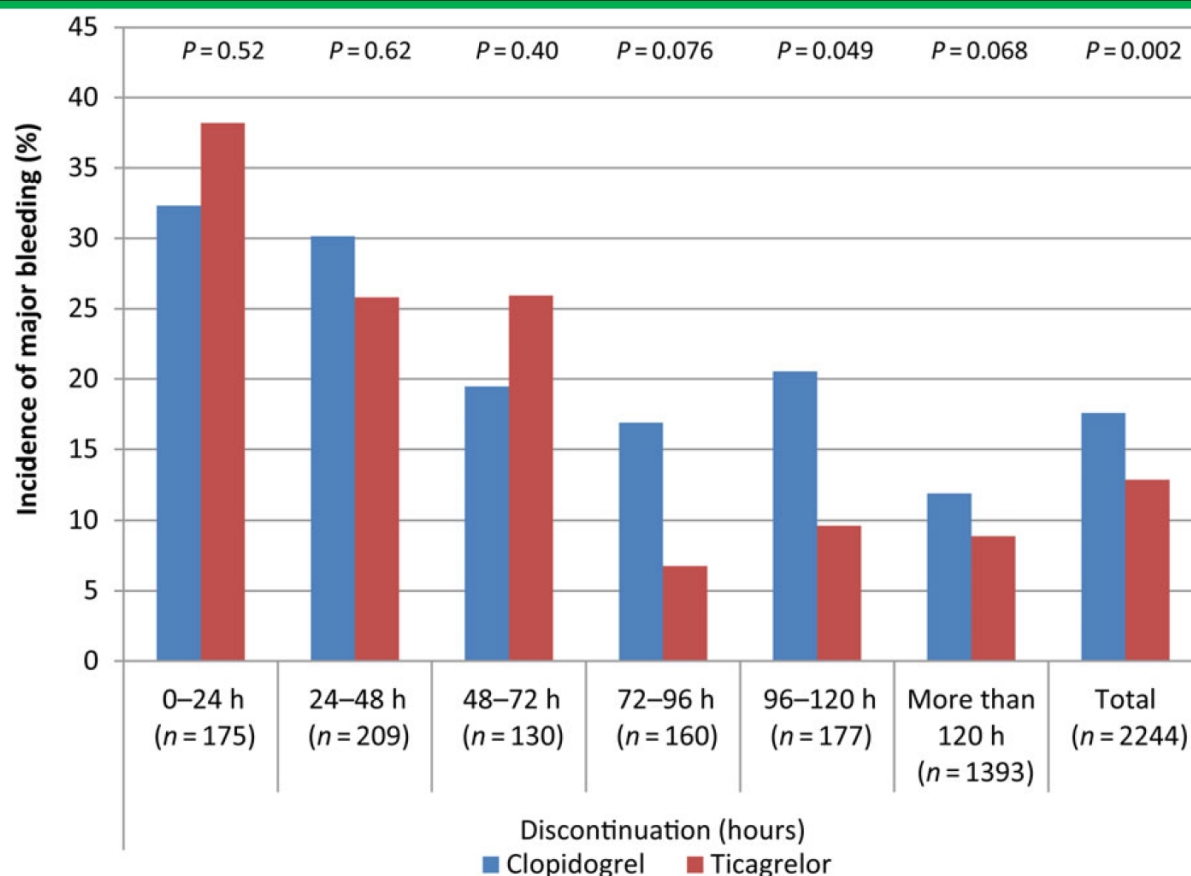
Figure 1. Platelet activation and mechanism of inhibition of ticagrelor and other platelet

Anticoagulants and antiplatelets: Cardiology dream ⇔ Perioperative nightmare

- ❖ People with acute coronary syndrome (ACS)
 - who have ischaemic electrocardiogram changes or elevation of cardiac troponin
 - should have immediate treatment with both aspirin (300 mg loading dose) and ticagrelor (180 mg loading dose).
- ❖ Ticagrelor in combination with low-dose aspirin is recommended for up to 12 months as a treatment option in adults with ACS with:
 - ST-elevation myocardial infarction that cardiologists intend to treat with primary percutaneous coronary intervention (PCI), or
 - non-ST-elevation myocardial infarction, or
 - admission to hospital with unstable angina.

Coronary artery bypass grafting-related bleeding complications in patients treated with ticagrelor or clopidogrel: a nationwide study

Emma C. Hansson¹, Lena Jidéus², Bengt Åberg³, Henrik Bjursten⁴, Mats Dreifaldt⁵, Anders Holmgren⁶, Torbjörn Ivert⁷, Shahab Nozohoor⁴, Mikael Barbu³, Rolf Svedjeholm⁸, and Anders Jeppsson^{1,9*}



❖ Definition of major bleeding

- death
- reoperation due to bleeding
- intracranial haemorrhage
- transfusion of 5 or more units of RBCs over 48 h,
- drainage > 2000 mL over 24 h

Salvage myocardial revascularisation in spontaneous left main coronary artery dissection with cardiogenic shock – the role of mechanical circulatory support

Ashok Padukone, Ahmed K. Sayeed, Nandor Marczin, Diana García Sáez, Bartłomiej Zych, Prashant N. Mohite, Mohamed Zeriouh, Robert D. Smith, Andre R. Simon, Anton Sabashnikov and Aron-Frederik Popov

Perfusion

2017, Vol. 32(2) 171–173

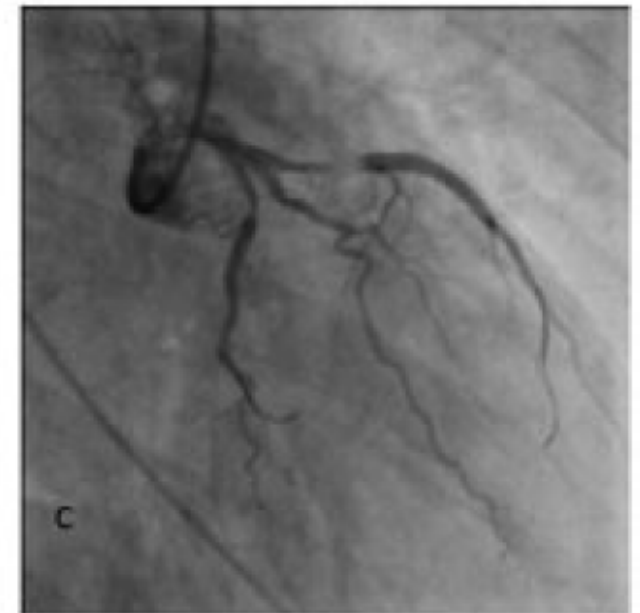
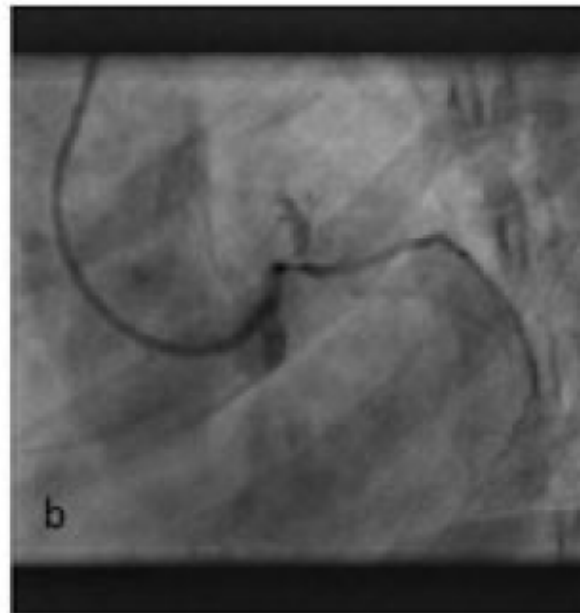
© The Author(s) 2016

Reprints and permissions:

sagepub.co.uk/journalsPermissions.nav

DOI: 10.1177/0267659116667803

journals.sagepub.com/home/prf



openheart Operative survival in patients with acute aortic disease in the era of newer oral anticoagulants

Johannes Lagethon Bjørnstad ^{1,2}, Adil Mahboob Khan,¹
Henriette Røed-Undlien,² Bjørn Bendz ^{2,3}, Ståle Nygård,⁴ Tom Nilsen Hoel,¹
Per Snorre Lingaas¹

Adjusted survival

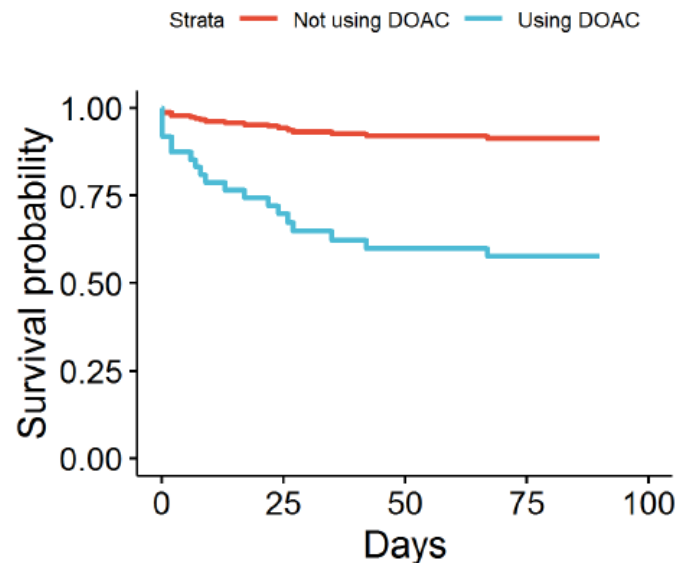


Table 4 Postoperative data by anticoagulant/platelet inhibitor. Patients not surviving the operation were excluded from the upper part of this table. (Single platelet inhibitor or less, warfarin, DAPT or DOAC.)

		Single platelet inhibitor or less	Warfarin	DAPT	DOAC
Number of operations	n	107	8	13	5
PO length of stay	days	4 (2)	4.5 (3)	7 (7)	3 (1)
PO ICU stay	days	2 (3)	2.5 (1.75)	2 (4.5)	1 (3)
PO ventilator >24 hour	%	23	25	23	50
PO reintubated	%	6	0	0	20
PO renal replacement therapy	%	4	0	15	0
PO circulatory support	%	0	0	8	0
PO bleeding	ml	660 (990)	615 (550)	820 (870)	820 (3246)
Any transfusion	%	96	100	92	100
erythrocytes	units	3 (4.75)	2 (2)	5 (4)	19 (21)
plasma	units	5 (5.75)	2.5 (3.25)	5 (4)	12 (20) * DOAC vs warfarin
thrombocytes	units	1 (1)	1 (1.25)	1 (3)	4 (6)
PO autotransfusion	%	32	38	15	75
PO autotransfusion	ml	0 (450)	0 (518)	0 (0)	591 (521)

Table I Reversal agents for anticoagulants

	Ciraparantag	Andexanet^a	Four-factor PCC^b	Idarucizumab^b
Structure	Synthetic water-soluble cationic small molecule	Inactive, Gla-domain-truncated, recombinant factor Xa	Contains prothrombin and factors VII, IX, and X	Humanized monoclonal antibody fragment
Molecular weight (Da)	512	39 000	50 000–72 000	47 766
Anticoagulants reversed	Direct oral anticoagulants (apixaban, dabigatran, edoxaban, and rivaroxaban) and heparin	Direct oral factor Xa inhibitors (apixaban, edoxaban and rivaroxaban) and heparin	Direct oral anticoagulants (apixaban, dabigatran, edoxaban, and rivaroxaban) and vitamin K antagonists	Dabigatran
Mechanism of action	Binds to direct oral anticoagulants and heparin via non-covalent hydrogen bonds and charge–charge interactions	Competitive binding to oral factor Xa inhibitors and competition with factor Xa for binding to heparin-catalysed antithrombin	Enhances factor Xa and thrombin generation	Binds free and thrombin-bound dabigatran
Administration	Single i.v. bolus	I.v. bolus followed by a 2 h infusion	I.v. infusion over 10–20 min	Single or double i.v. bolus
Storage	Room temperature	Refrigerated	Refrigerated or room temperature	Refrigerated
Cost	Probably low	Very high	Moderate	Moderate

Original Articles

STS/SCA/AmSECT/SABM Update to the Clinical Practice Guidelines on Patient Blood Management

Pierre Tibi, MD;^a R. Scott McClure, MD, FRCSC;^b Jiapeng Huang, MD;^c Robert A. Baker, PhD, CCP;^d David Fitzgerald, DHA, CCP;^e C. David Mazer, MD;^f Marc Stone, MD;^g Danny Chu, MD;^h Alfred H. Stammers, MSA, CCP Emeritus;ⁱ Tim Dickinson, CCP;^j Linda Shore-Lesserson, MD;^k Victor Ferraris, MD;^l Scott Firestone, MS;^m Kalie Kissoon;^m Susan Moffatt-Bruce, MD, FRCSCⁿ

❖ Preoperative anticoagulants (Class IIA, Level C–LD)

- In patients in need of emergent cardiac surgery with recent ingestion of a nonvitamin K oral anticoagulant (NOAC) or
- laboratory evidence of a NOAC effect,
- administration of the reversal antidote specific to that NOAC is recommended
 - i.e., administer **idarucizumab** for **dabigatran** at appropriate dose or
 - administer **andexanet-a** for either **apixaban** or **rivaroxaban** at an appropriate dose).

❖ If the antidote for the specified NOAC is not available, **prothrombin concentrate is recommended,**

- recognizing that the effective response may be variable.



ESC

European Society
of Cardiology

European Heart Journal (2022) 43, 985–992
<https://doi.org/10.1093/eurheartj/ehab637>

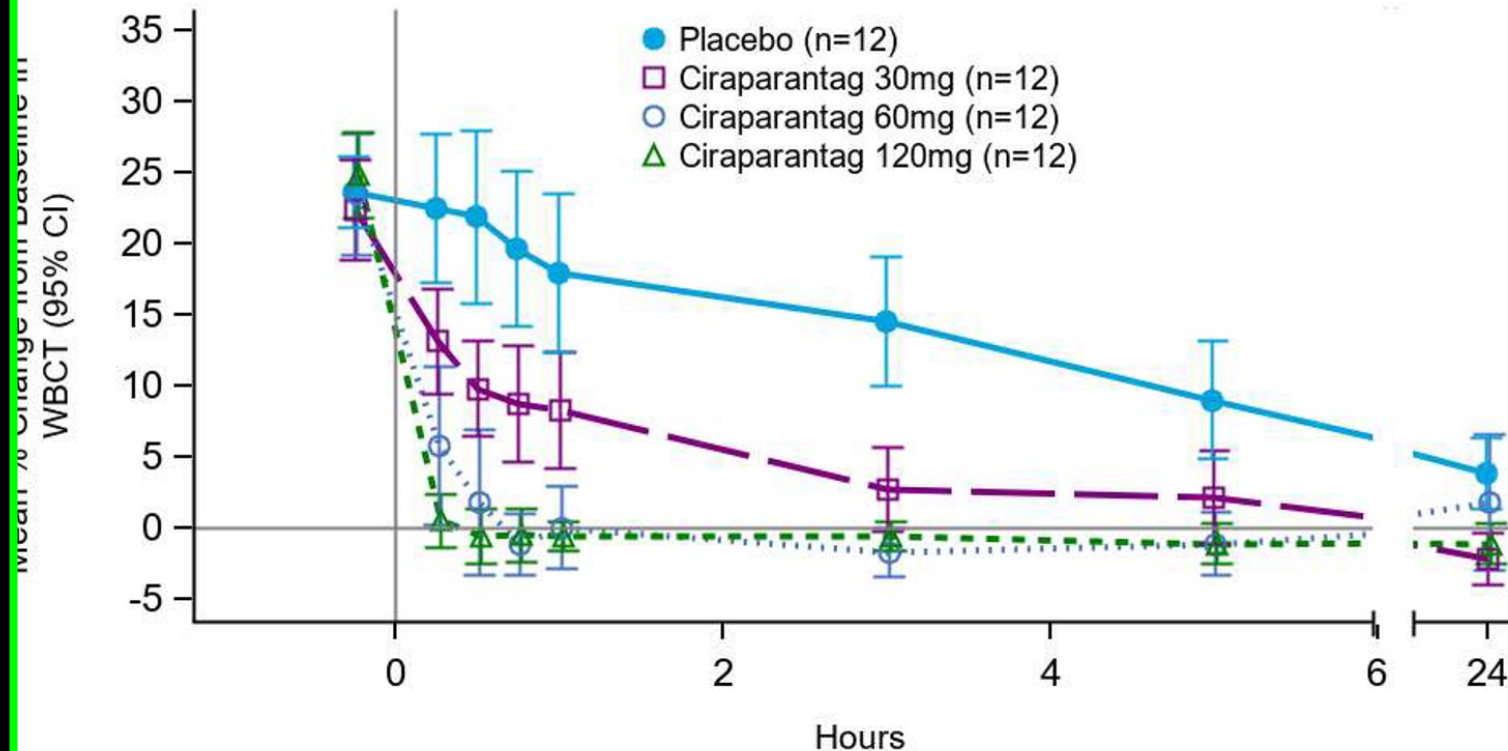
CLINICAL RESEARCH

Thrombosis and antithrombotic treatment

Ciraparantag reverses the anticoagulant activity of apixaban and rivaroxaban in healthy elderly subjects

Jack Ansell ^{1*}, Sasha Bakhru ², Bryan E. Laulicht ³, Gregory Tracey ⁴, Stephen Villano ⁵, and Daniel Freedman ⁵

Apixaban





ESC

European Society
of Cardiology

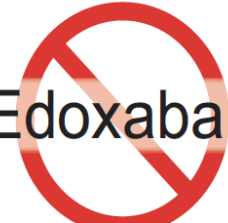
European Heart Journal (2022) 43, 993–995
<https://doi.org/10.1093/eurheartj/ehab706>

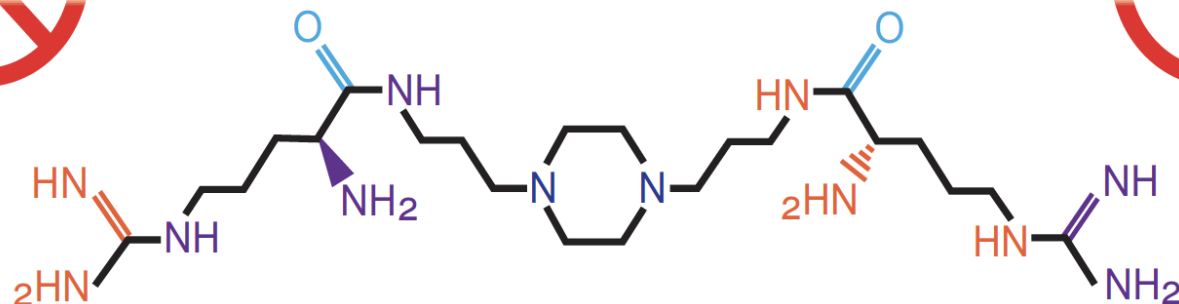
EDITORIAL

Ciraparantag as a potential universal anticoagulant reversal agent

Noel C. Chan and Jeffrey I. Weitz *

 Apixaban

 Edoxaban



Ciraparantag

 Enoxaparin

 Rivaroxaban

Graphical Abstract Ciraparantag binds to apixaban, edoxaban, enoxaparin, and rivaroxaban and reverses their anticoagulant activity.

BENTRACIMAB (PB2452)

A novel ticagrelor reversal agent to treat or prevent
major bleeding

REVERSE-IT

Rapid and SustainEd ReVERSAl of TicagrElor – Intervention Trial

REVERSE-IT

- ❖ Design: Phase 3, multi-center, open-label, prospective single-arm trial
- ❖ Aim: reversal of the antiplatelet effects of ticagrelor with bentracimab in patients who present with uncontrolled major or life-threatening bleeding or who require urgent surgery or invasive procedure.
- ❖ Interim analysis Nov 2021:
 - Bentracimab achieved primary reversal endpoint with immediate and sustained reversal of the antiplatelet effects of ticagrelor in both surgical and bleeding populations;
 - Co-primary endpoint of clinical hemostasis achieved in greater than 90% of patients;
 - Bentracimab appeared well tolerated with no drug-related serious adverse events.

NEW OPPORTUNITIES FOR CARDIAC SURGERY BY CYTOSORB THERAPY

High Risk
Cardiac surgery
REFRESH II ...

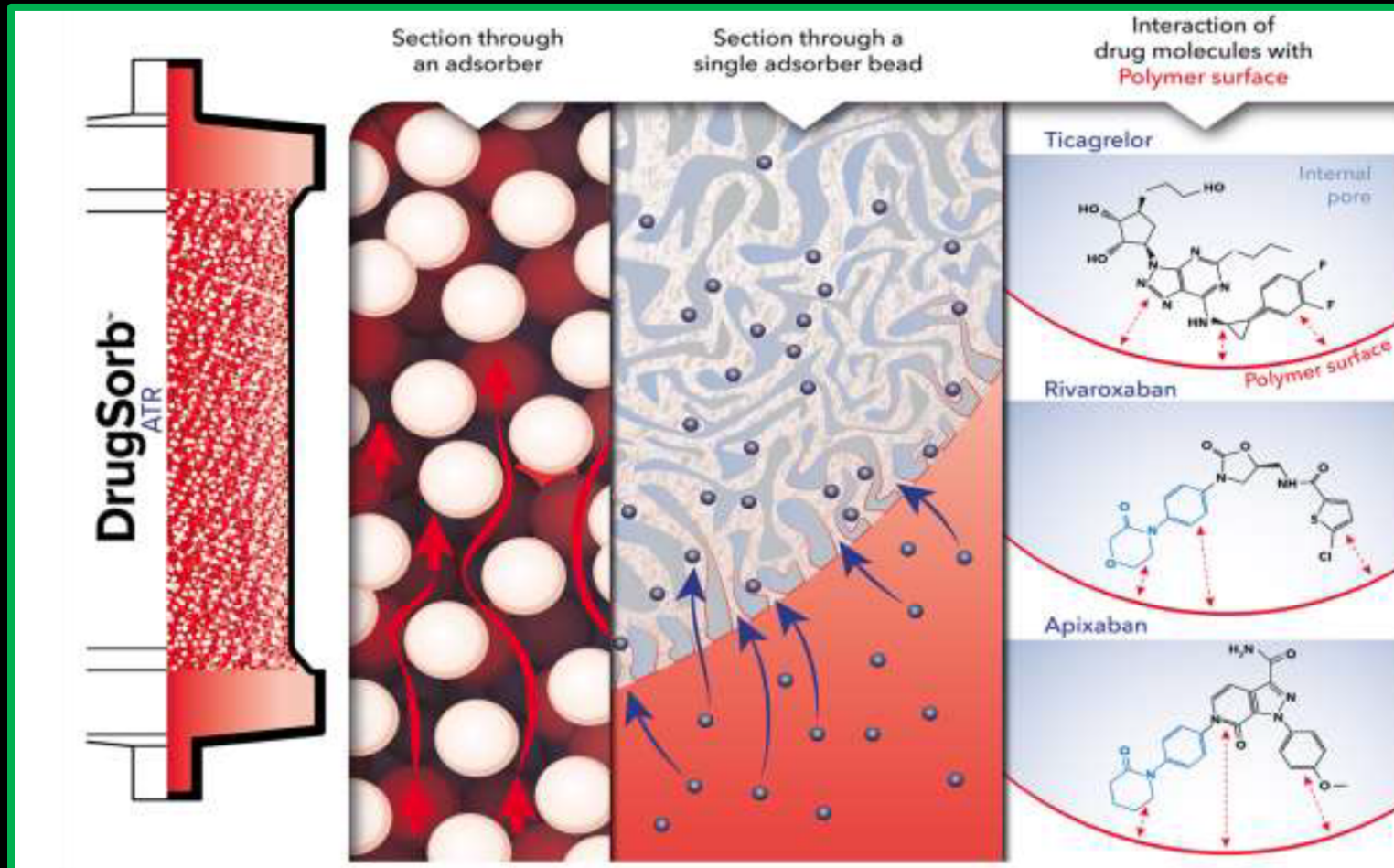


Heart failure
LVAD

Endocarditis
REMOVE...

Heart
Transplant

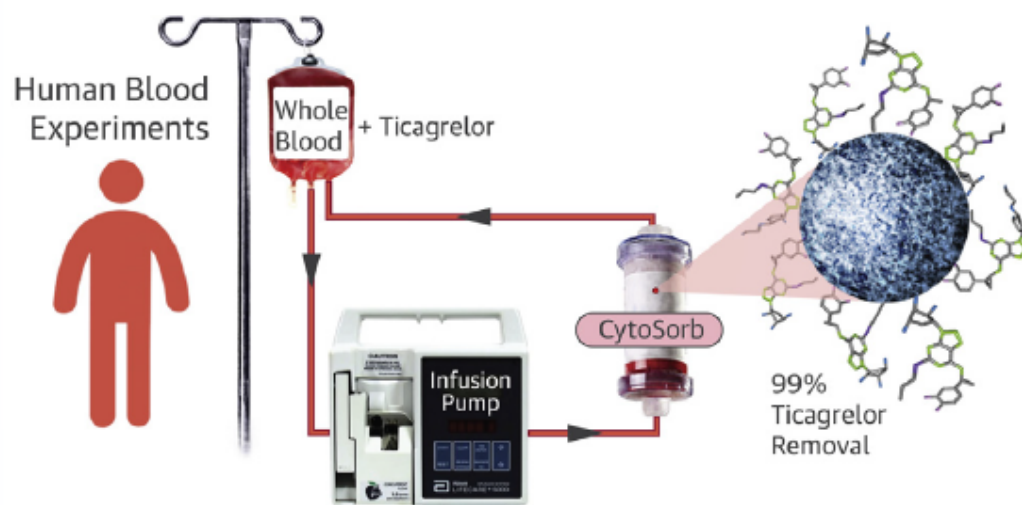
DrugSorb™-AntiThrombotic Removal (ATR) haemoadsorption



PRECLINICAL RESEARCH

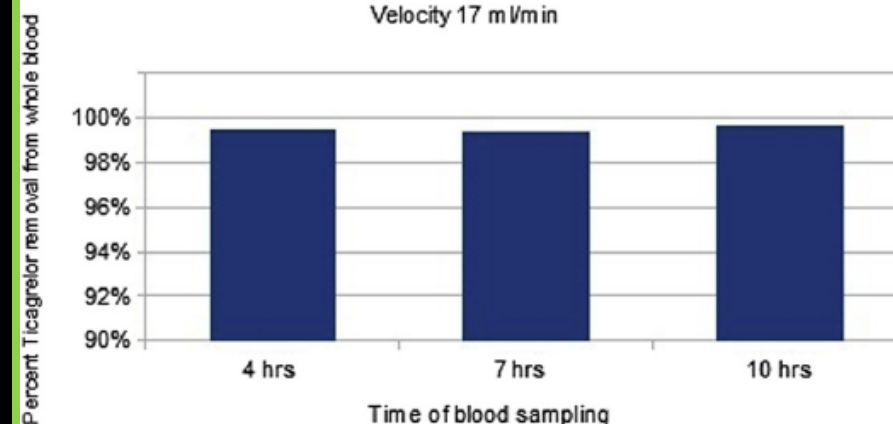
Ticagrelor Removal From Human Blood

George O. Angheloiu, MD,^{a,b,c} Gabriel B. Gugiu, PhD,^d Cristian Ruse, PhD,^e Rishikesh Pandey, PhD,^a
Ramachandra R. Dasari, PhD,^a Carl Whatling, PhD^f



B Removal of Ticagrelor on a CytoSorb 300 cc column

Velocity 17 m l/min



Apixaban removal “in vitro”

Journal of Cardiothoracic and Vascular Anesthesia 36 (2022) 1636–1644

Contents lists available at ScienceDirect

Journal of Cardiothoracic and Vascular Anesthesia

journal homepage: www.jcvaonline.com

Original Article

In Vitro Apixaban Removal By CytoSorb Whole Blood Adsorber: An Experimental Study

Henriette Røed-Undlien, MD^{*},
Nina Haagenrud Schultz, MD, PhD^{†,‡,§}, Asbjørn Lunnan, MSc^{||},
Inger Marie Husebråten, MSc^{||}, Birgit Malene Wollmann, MSc[#],
Espen Molden, MSc, PhD^{*,||},
Johannes Lagethon Bjørnstad, MD, PhD^{*,||,†}

^{*}Institute of Clinical Medicine, University of Oslo, Oslo, Norway

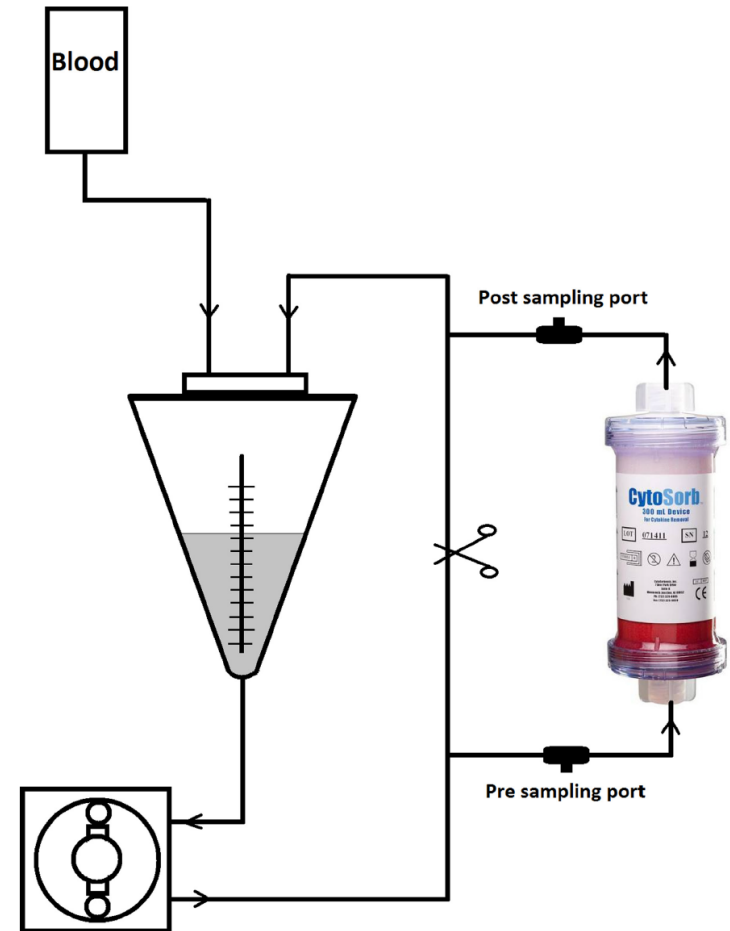
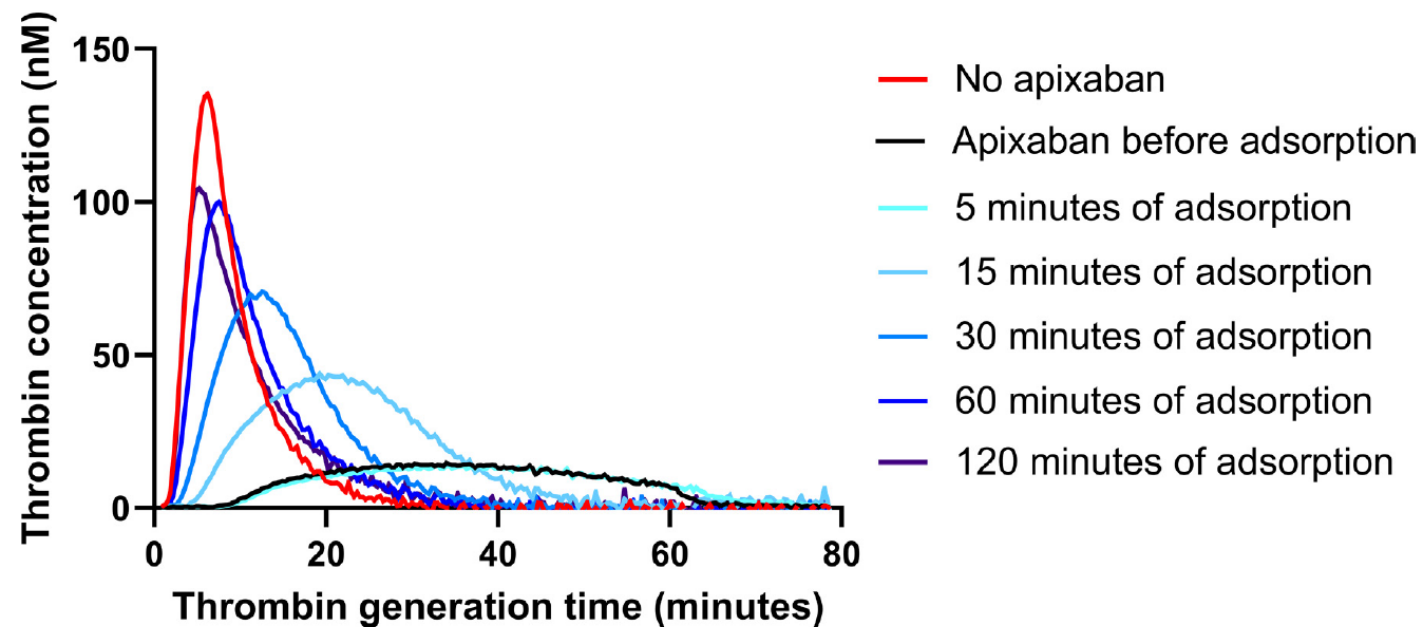
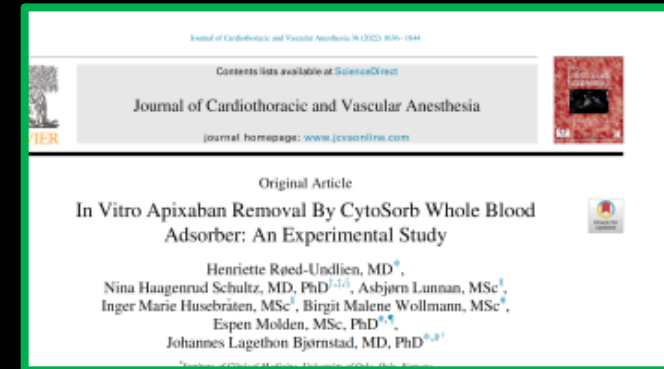
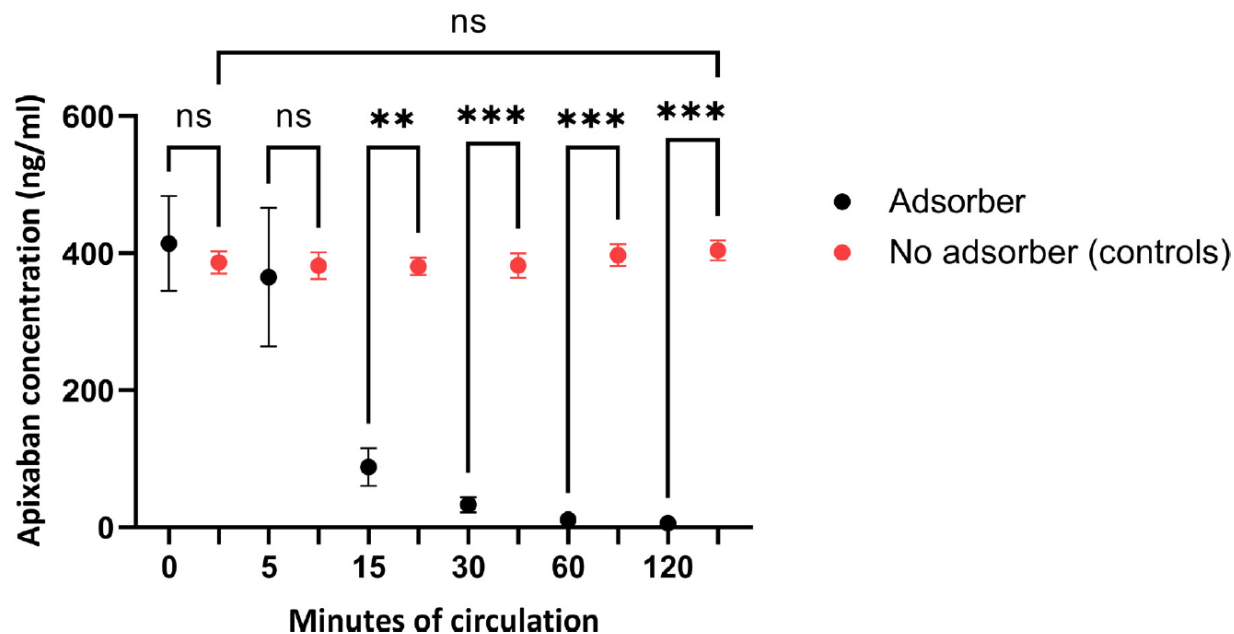
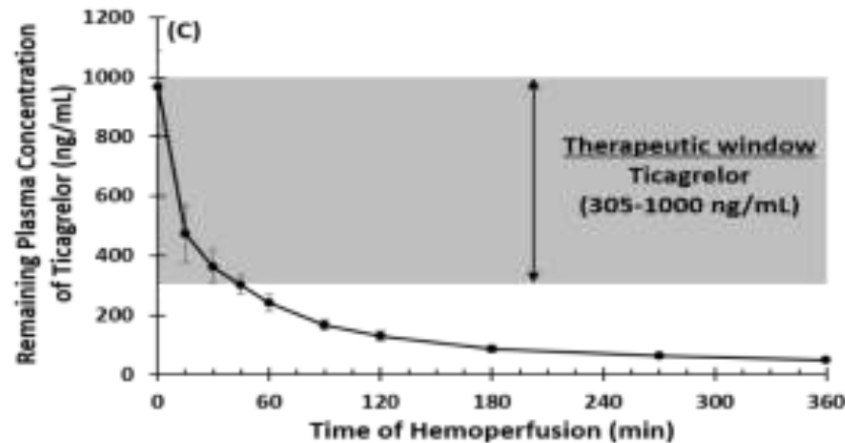
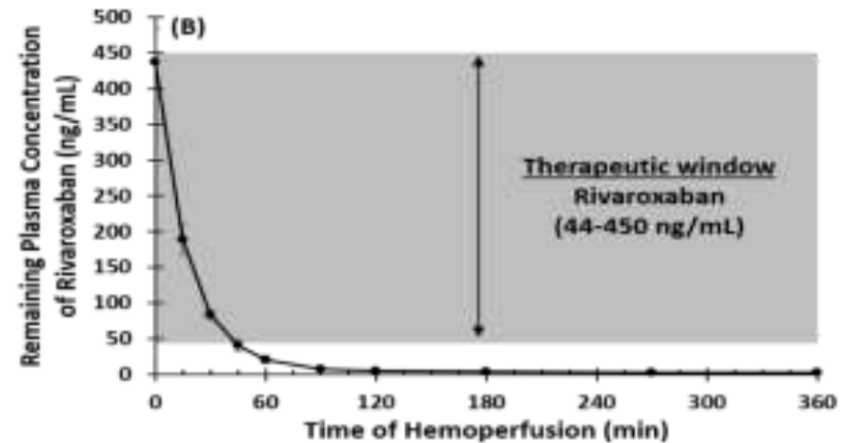
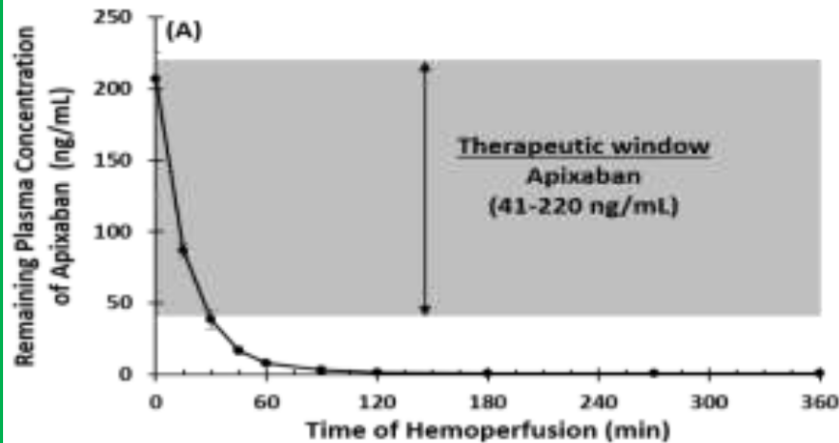


Fig. 1. The CytoSorb whole blood adsorber was connected to the circuit. The flow was kept at 300 mL/min.



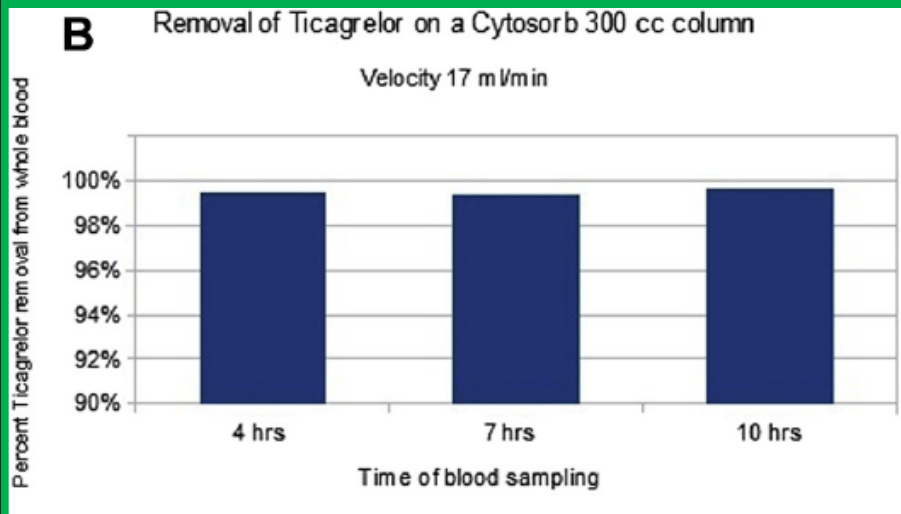
DrugSorb™-AntiThrombotic Removal (ATR) haemoadsorption



PRECLINICAL RESEARCH

Ticagrelor Removal From Human Blood

George O. Angheloiu, MD,^{a,b,c} Gabriel B. Gugiu, PhD,^d Cristian Ruse, PhD,^e Rishikesh Pandey, PhD,^a
Ramachandra R. Dasari, PhD,^a Carl Whatling, PhD^f



PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Our method could be applied during a clinical scenario that may involve a patient loaded with ticagrelor in the emergency department, undergoing cardiac catheterization and then referred immediately to open heart surgery. Ticagrelor removal would start and continue through surgery, mostly because the patient will be on a cardiopulmonary bypass machine, which would allow continuous recirculation of the blood through the sorbent column. In a second sce-

CytoSorb for reducing risk of bleeding during cardiac surgery

Medtech innovation briefing

Published: 2 February 2021

www.nice.org.uk/guidance/mib249

WHY SHOULD NHS HOSPITALS COMPLY WITH NICE GUIDANCE?



NHS Standard Contract 2020/21 Service Conditions (Full Length)

Prepared by: NHS Standard Contract Team, NHS England
nhs.sc.contractshelp@nhs.net
(please do not send contracts to this email address)

Version number: 1

First published: March 2020

Publication Approval Number: 001588

NHS STANDARD CONTRACT 2020/21 SERVICE CONDITIONS (Full Length)

2.1.4	consider and respond to the recommendations arising from any audit, Serious Incident report or Patient Safety Incident report;	
2.1.5	comply with the standards and recommendations issued from time to time by any relevant professional body and agreed in writing between the Co-ordinating Commissioner and the Provider;	
2.1.6	comply, where applicable, with the recommendations contained in NICE Technology Appraisals and have regard to other Guidance issued by NICE from time to time;	
2.1.7	respond to any reports and recommendations made by Local Healthwatch; and	
2.1.8	meet its obligations under Law in relation to the production and publication of Quality Accounts.	
2.2	The Provider must comply with all applicable EU Exit Guidance.	All
2.3	The Parties must comply, where applicable, with their respective obligations under, and with recommendations contained in, MedTech Funding Mandate Guidance.	All
SC3 Service Standards		

How to use NICE products

How can I... ?

NICE guidance

Evidence-based recommendations developed by independent committees, including professionals and lay members, and consulted on by stakeholders

NICE guidance aims to give everyone access to high-quality care and provide best value for the NHS and social care

It helps new treatments and technologies to be made available in the NHS and care sector

It helps professionals and people using services make informed decisions about care

NICE standards and indicators

Support quality improvement and delivery of high-quality care, based on NICE or NICE-accredited guidance

NICE guidelines
Review the evidence across broad health and social care topics

Find out about best care across health and social care topics

Find out if a new medical device is a good use of NHS resources

Medical technologies guidance
Review new medical devices for adoption in the NHS

Technology appraisal guidance
Review clinical and cost effectiveness of new treatments

Find out if a treatment must be available for a specific condition

Find out if a diagnostic device or tool is a good use of NHS resources

Diagnostics guidance
Review new diagnostic technology for adoption in the NHS

Highly specialised technologies guidance
Review clinical and cost effectiveness of specialised treatments

Find out if a treatment must be available for a rare condition

Find out if a procedure is safe and effective to use in the NHS

Interventional procedures guidance
Review the efficacy and safety of procedures

Quality standards
Set out priority areas for quality improvement in health and social care

Measure services and identify areas for improvement

Create a local performance dashboard to assess local services

NICE indicator menu
Measures based on outcomes or processes for health and care

Medtech innovation briefings

- ❖ Medtech innovation briefings (MIBs) are NICE advice.
- ❖ They are designed to support NHS and social care commissioners and staff who are considering using new medical devices and other medical or diagnostic technologies.
- ❖ MIBs are designed to be fast, flexible and responsive to the need for information on innovative technologies.
- ❖ They help avoid the need for organisations to produce similar information locally, saving staff time and resources.

Medtech innovation briefings

- ❖ The information provided in a briefing includes:
 - a description of the technology
 - how the technology is used
 - the potential role in the treatment pathway
 - a review of relevant published evidence
 - the likely costs of using the technology.

Table 2: Studies investigating the hemadsorption of antiplatelets/anticoagulants by Cytosorb in myocardial surgical revascularisation

Reference	Study Design	Study Location	Type of Cardiac Surgery	Removal	Study Size (n)	Interventions and Control
Hassan et al., 2019	Non-randomised observational study with retrospective comparison to controls	Germany	Emergency cardiac surgery. CABG: 89.1% CABG + valve: 9.1%	Ticagrelor (n=43) or rivaroxaban (n=12)	55	Cytosorb adsorption versus no hemadsorption
Mair et al., 2020	Case study	Germany	Urgent off-pump CABG	Ticagrelor and rivaroxaban	1	Cytosorb, absorption. No control.
Hassan et al., 2020a*	Observational study	Germany	Emergency isolated CABG only.	Ticagrelor	55	Cytosorb, absorption. No control.
Hassan et al., 2020b*	Bootstrap analysis of a retrospective case series	Germany	Emergency cardiac surgery (type not specified).	Ticagrelor	43	Cytosorb adsorption versus no hemadsorption
Bradic et al., 2020*	Observational study with controls	Croatia	Emergency cardiac surgery (type not specified).	Ticagrelor (n=19) or rivaroxaban (n=12) or dabigatran (n=3)	34	Cytosorb absorption versus no hemadsorption

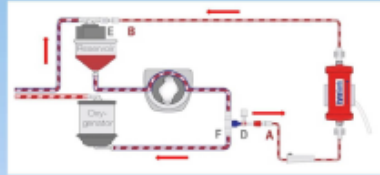
CYTOSORB ADSORPTION OF DIRECT ORAL ANTICOAGULANTS IN PATIENTS AT HIGH RISK OF BLEEDING DURING CARDIAC SURGERIES



Nikola Bradic^{1,2}, Zdenko Povsic – Cevra³

1. Clinic of Anesthesiology, Resuscitation and Intensive Care Medicine, Department for Cardiovascular Anesthesiology and Cardiac Intensive Medicine, University Hospital Dubrava, Zagreb, Croatia, EU
2. University North, Department of Biomedical Sciences, Varaždin, Croatia, EU
3. Department for Anesthesiology and Intensive Care, Magdalena Special Hospital for Cardiovascular Surgery and Cardiology, Krapinske Toplice, Croatia, EU

BACKGROUND: To analyze the results of use of CytoSorb adsorption filter (CytoSorbents gmbh, USA) during open-heart surgeries in patients which have used direct oral anticoagulants (DOAC) during preoperative period. Patients who used different types of DOACs are in great risk of perioperative bleeding. Withdrawal few days before surgery could not prevent serious perioperative bleeding, especially in emergency operations. Several case reports and recent studies have shown positive effect of CytoSorb filter on DOACs' purification from circulating blood. During extracorporeal circulation (ECC), filter decreases its effect and risk of bleeding.



METHODS: We compared patients who underwent cardiac surgery and received preoperative DOAC therapy between January 2016 and September 2019. Total number of patients was 34. They divided in G 1 with 12 pts. (35% of all) which did not treated with CytoSorb filter, and in G 2, in which were 22 pts. (65%) treated with filter, installed in ECC machine. In both groups, it was analyzed as follows: type of surgery (elective or emergency); total amount of blood loss; need for re sternotomy; need for transfusions of blood and blood products; length of stay in intensive care unit (ICU).

LITERATURE:

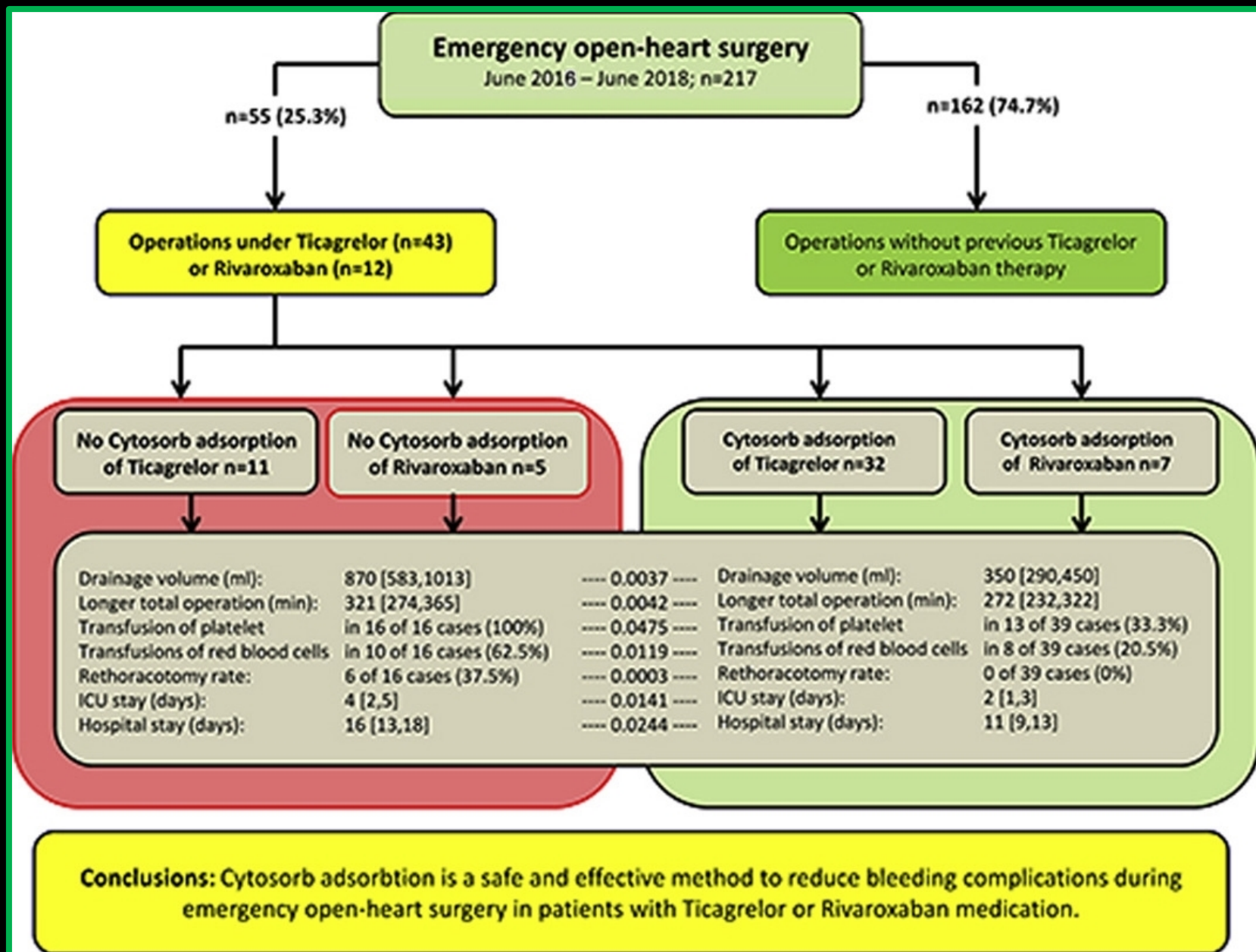
1. Jansardakul M, Trevar M, Wenzel MR, et al. Ticagrelor Removal by CytoSorb® in Patients Requiring Bypass or Urgent Cardiac Surgery: A UK-Based Cost-Utility Analysis Pharmacokinetics - Open <https://doi.org/10.1007/s12168-019-00183-w>
2. Hironaka PM, David C, Allos R, et al. New alternative to antidotes for novel oral anticoagulants and ticagrelor in the case of severe bleeding. Critical Care (2020) 24:40 <https://doi.org/10.1186/s13054-020-2768-7>
3. Koertge A, Wesselschmidt R, Wild T, Bittner S. Extracorporeal Hemoperfusion as a Potential Therapeutic Option for Critical Accumulation of Rivaroxaban. Blood Purif 2016;45:126-129

RESULTS: Of 12 patients in G1, 6 patients (50%) received ticagrelor (2 had emergency surgery), 4 (33%) rivaroxaban and 2 dabigatran (17%, emergency pts.). In G2, of 22 pts. 13 (59%) received ticagrelor (5 were emergency), 8 pts. (36%) rivaroxaban (2 were emergency) and 1 (5%) dabigatran (emergency). Comparing between groups, patients in G1 had (in average values): longer total time of surgery (310 vs 240 min); higher average amount of drainage volumes in first 24 hours (1200 vs. 320 mL); more transfusions of red blood cells (950 vs 250 mL); transfusions of platelets (800 vs 150 mL); transfusions of fresh frozen plasma (1180 vs 620 mL); in more than half patients in G1 (58.3%) was indication for re sternotomy, versus 18.2% in G2. ICU length of stay was longer in G1 (approx. 5.3 vs. 2.4 days).

	Total	G1 (n)	G2 (n)
n	34	12	22
ticagrelor	19 (56%)	6	13
rivaroxaban	12 (35.2%)	4	8
dabigatran	3 (8.8%)	2	1

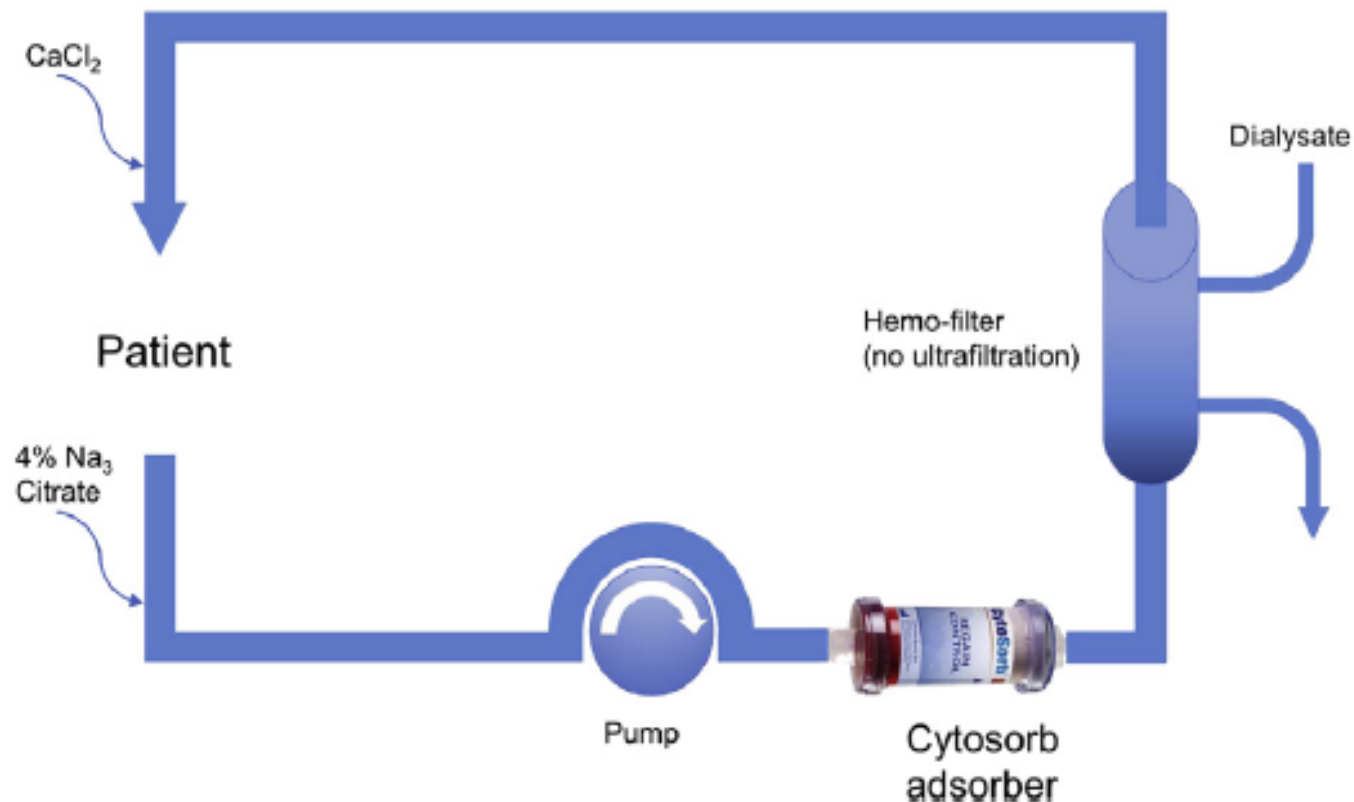
CONCLUSIONS: These results have shown favorable effect of CytoSorb filter usage in patients who are preoperatively receiving DOACs' medications. During ECC, depends on flow, filter can, in short time, adsorbs medications which could be still active in serum. This is important both in emergency and elective surgeries. It is known that DOAC effect could be prolonged in older patients, and especially in patients with renal and liver dysfunction. In those cases, effects of DOACs' can be prolonged for the several days. Usage of CytoSorb filter decreases DOAC effect, and consequently, the risk of perioperative bleeding. Further, decreases the needs for giving blood and blood products, length of ICU stay, and finally, overall costs of patients' management.

- ❖ Total time of surgery (310 vs. 240 min)
- ❖ Drainage in 24 hours (1200 vs. 320 mL)
- ❖ Transfusions:
 - red blood cells (950 vs 250 mL)
 - platelets (800 vs 150 mL)
 - fresh frozen plasma (1180 vs 620 mL).
- ❖ Resternotomy 58.3% vs. 18.2%
- ❖ ICU length of stay 5.3 vs. 2.4 days



Ticagrelor and Rivaroxaban Elimination With CytoSorb Adsorber Before Urgent Off-Pump Coronary Bypass

Helmut Mair, MD, Clemens Jilek, MD,
Brigitte Haas, MD, and Peter Lamm, MD




Overall assessment of the evidence

- ❖ The **innovative aspects** are that it is the **first medical device** that can be used to remove ticagrelor from the blood during urgent or emergency cardiac surgery.
- ❖ Using CytoSorb
 - ❖ in emergency cardiac surgery could reduce resource use for management of bleeding complications, and
 - ❖ in urgent cardiac surgery could reduce length of hospital stay before the procedure and the use of adjunctive bridging treatments.
- ❖ Using CytoSorb to remove ticagrelor during surgery is a safe and effective method to reduce bleeding complications.



Ticagrelor Removal by CytoSorb® in Patients Requiring Emergent or Urgent Cardiac Surgery: A UK-Based Cost-Utility Analysis

Mehdi Javanbakht^{1,5}  · Miranda Trevor² · Mohsen Rezaei Hemami³ · Kazem Rahlmi⁴ · Michael Branagan-Harris⁵ · Fabian Degener⁶ · Daniel Adam⁶ · Franziska Prellsing⁶ · Jörg Scheler⁶ · Suzanne F. Cook⁷ · Eric Mortensen⁸

- ❖ First economic evaluation of an intra-operative intervention to manage bleeding risk for patients on ticagrelor who would require emergent or urgent cardiac surgery in the NHS (based on clinical data mainly from Germany)
- ❖ In **emergent cardiac surgery** patients on ticagrelor, CytoSorb is associated with **significant cost-savings** in hospital resource utilisation (-£3,982)
- ❖ In **urgent patients**, CytoSorb allows **surgery to be performed 3-7 days earlier** and is likely to be cost saving

Overall assessment of the evidence

❖ Evidence includes

- 4 observational studies, of which 3 had a comparator group, 1 bootstrap analysis based on a retrospective case series and
- 1 case study
- Total n= 209 people

❖ The evidence is of low methodological quality

❖ All the studies are small in terms of patient numbers.

❖ All studies were done in Germany, apart from 1 that was done in Croatia, none in the UK

❖ Further evidence is needed with a large sample size.

Hemoadsorption of Rivaroxaban and Ticagrelor during Acute Type A Aortic Dissection Operations

Karim Hossain,¹ Tobias Bräutig,² Michael Casper,² Peter Woblmuth,² Holger Pösch,¹ Michael Schenckel,¹ and Stephan Gude¹

Objective: To analyze the results of hemoadsorption in patients with cardiac surgery to thoracic aortic surgery, who had been loaded beforehand with either Factor Xa inhibitor rivaroxaban or P2Y₁₂ receptor antagonist ticagrelor.

Methods: We investigated 21 of 171 consecutive patients (median age 71 [interquartile range 62, 76] years) who underwent emergency cardiac operations for acute type A aortic dissection between 2014 and 2020. These patients were pretreated with rivaroxaban (n = 9) or ticagrelor (n = 12). In ten of 21 cases (since 2017), we installed a hemoadsorber into the heart-lung machine and compared the results to eleven patients done without hemoadsorber before that time.

Results: The operation time was significantly shorter in the adsorber group (286 ± 40 min vs. 348 ± 79 min; p = 0.045). The postoperative 24-hour drainage volume was significantly lower after adsorption (p < 0.001; 482 ± 122 ml vs. 907 ± 427 ml) and no rethoracotomy had to be performed (compared to two rethoracotomies [18.9%] among patients without adsorber use). Also, patients without hemoadsorption required significantly more platelet transfusion (p = 0.045).

Conclusions: In patients with acute type A aortic dissection who were pretreated with rivaroxaban and ticagrelor, the intraoperative use of Cytosorb hemoadsorption during cardiopulmonary bypass is reported for the first time. The method was found to be effective to prevent from bleeding and to improve the outcome in aortic dissection.

Keywords: aortic dissection, aortic surgery, bleeding complications, cardiac surgery, type A aortic dissection

Table 2 Details of surgery and early postoperative data

	Non-adsorber group (n = 11)	Adsorber group (n = 10)
Surgery procedure, n (%)		
Ascending replacement	11 (100)	10 (100)
Hemiarch replacement	3 (27.3)	2 (20.0)
Total arch replacement	3 (27.3)	2 (20.0)
Coronary bypass	3 (27.3)	0 (0)
Time-related outcomes, mean ± SD		
BPT, min	203 ± 65	207 ± 45
ACC, min	141 ± 80	143 ± 45
Procedure time, min	348 ± 79	286 ± 40
Transfusion of platelet, n (%)		
0	1 (9.1)	4 (40.0)
>1	10 (90.9)	6 (60.0)
Transfusion of red blood cells, n (%)		
0	3 (27.3)	4 (40.0)
>1	8 (72.8)	6 (60.0)
Outcome data, median (IQR)		
Drainage volume/24 h (ml)	750 [635, 965]	475 [428, 508]
Days in intensive care	9 [6, 10.5]	4 [4.0, 9.0]
Total length of stay, days	15 [14, 16]	16 [12, 23]
Rethoracotomy rate, n (%)	2 (18.2)	0 (0)
30-day death, n (%)	3 (27.3)	1 (10.0)

BPT: bypass time; ACC: aortic clamping time; SD: standard deviation; IQR: interquartile range

Use of the CytoSorb® filter for elimination of residual therapeutic argatroban concentrations during heparinized cardiopulmonary bypass for heart transplantation

Andreas Koster,¹  Helmuth Warkentin,¹ Vera von Dossow¹ and Michiel Morshuis²

Perfusion

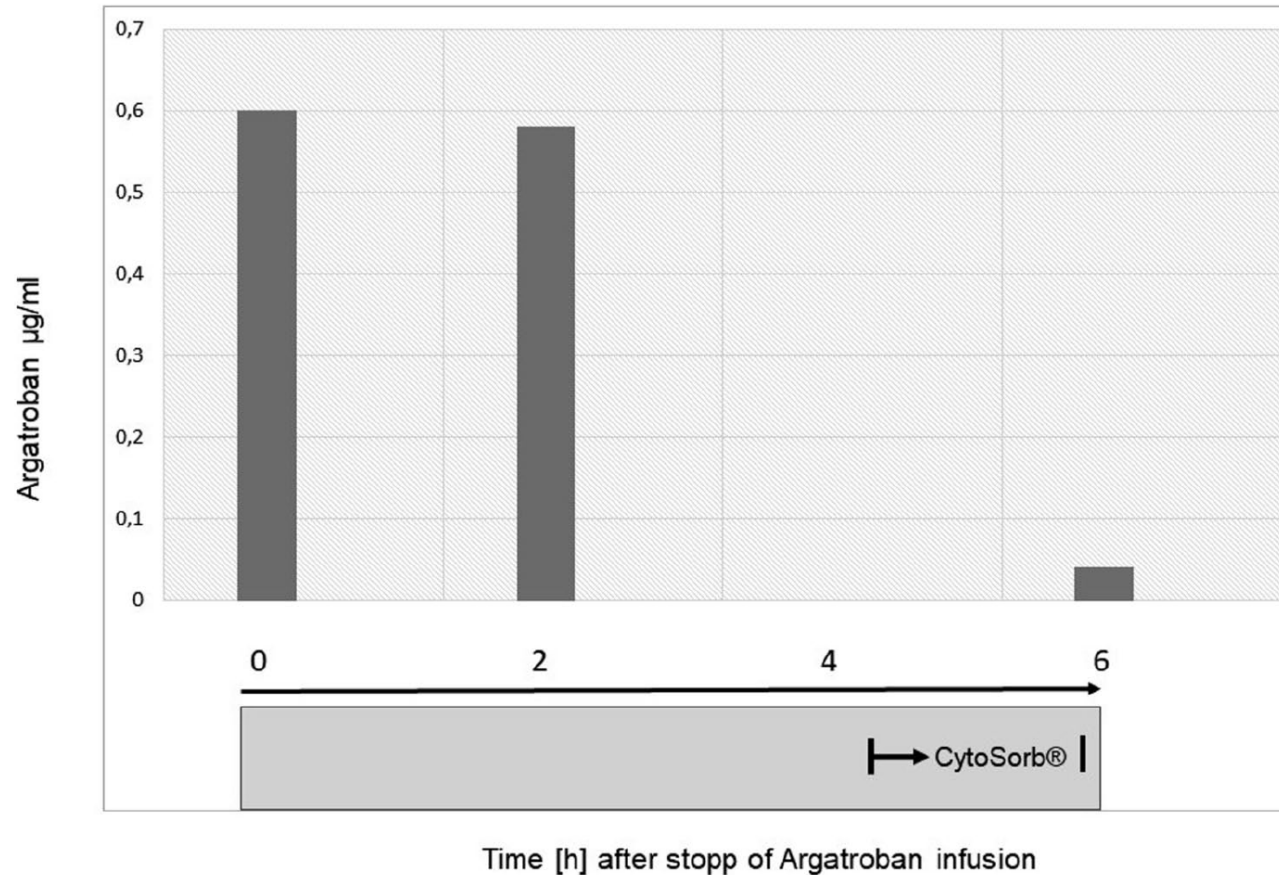
1-4

© The Author(s) 2022

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/02676591221093875

journals.sagepub.com/home/prf

TISORB UK Study

❖ Ticagrelor CytoSorb Hemoadsorption (TISORB):

- Prospective, Open, Multi-center, Single-arm Study (UK)
- to Demonstrate the Feasibility of the CytoSorb® 300 mL Device to Remove Ticagrelor During Cardiopulmonary Bypass
- in Patients on Ticagrelor Undergoing Emergent or Urgent Cardiothoracic Surgery

❖ Primary pharmacodynamic endpoint

- Change in platelet reactivity immediately before and after cardiopulmonary bypass

❖ Primary pharmacokinetic endpoint

- Change in ticagrelor blood concentration



STAR REGISTRY

(Safe and Timely Antithrombotic Removal - STAR)

International Registry on the Use of CytoSorb for Removal of Antithrombotic Agents in the Acute Hospital Setting

STAR Registry: Design & Protocol

❖ Study Type:

- Registry Study (observational, retro- and prospective data entry)

❖ Enrollment:

- 500 patients (anticipated) in total (all sites)
- Sep 2021 until Sep 2025

❖ Aim:

- Real-world clinical use patterns and associated clinical outcomes with the use of CytoSorb for the removal of antithrombotic agents
- **Clinical data only derive from standard clinical care;**

STAR Registry: Primary Outcome

- ❖ Bleeding complications including requirements for transfusions and other blood products assessed until postoperative day (POD) 3,
- ❖ Date of ICU discharge, or date of death, whatever comes first; on average 3 days

Rationale and design of the safe and timely antithrombotic removal - ticagrelor (STAR-T) trial: A prospective, multi-center, double-blind, randomized controlled trial evaluating reductions in postoperative bleeding with intraoperative removal of ticagrelor by the drugsorb™-ATR device in patients undergoing cardiothoracic surgery within 48 hours from last ticagrelor dose



C. Michael Gibson, MD^a, Michael J. Mack, MD^b, Victoria T. Lee, MD^c, David J. Schneider, MD^d, Frank W. Sellke, MD^e, E. Magnus Ohman, MD^f, Vinod H. Thourani, MD^g, Gheorghe Doros, PhD^{a,h}, Hans Kroger, MScⁱ, Donald E. Cutlip, MD^j, and Efthymios N. Deliargyris, MD^k *Boston, MA*

STAR-T N = 120

Patients requiring
CT surgery on CPB
within 48 hours from
last ticagrelor dose
Stratification by:

- a) Site, and
- b) Type of surgery

1:1

DOUBLE BLIND

DrugSorb™ -ATR + SOC

CPB Duration

Key Secondary Endpoint:
Post- vs. Pre-CPB Δ [ticagrelor]

Follow-up is through 30 days post-index operation

Intraoperative period

Postoperative period

SOC

Primary composite endpoint*:

Fatal bleeding events
UDPB \geq 2 events
24hr chest tube drainage

SOC

POD #2

(fatal bleeding events are
measured through 48hrs post-
op; UDPB through day 1 post-op)

...Day 30
Follow-up

*Ranked, utilizing the Win Ratio for analysis

NEWS

CYTOSORBENTS CORPORATION



FIRST PATIENT ENROLLED IN U.S. STAR-D PIVOTAL TRIAL EVALUATING THE DRUGSORB™-ATR ANTITHROMBOTIC REMOVAL SYSTEM TO REMOVE APIXABAN AND RIVAROXABAN DURING CARDIOTHORACIC SURGERY

MONMOUTH JUNCTION, N.J., April 29, 2022 /PRNewswire/ — [CytoSorbents Corporation](#) (NASDAQ: CTSO), a leader in the treatment of life-threatening conditions in intensive care and cardiac surgery using blood purification via its proprietary polymer adsorption technology, announced today that the first patient has been enrolled in the Safe and Timely Antithrombotic Removal-Direct Oral Anticoagulants (STAR-D) double-blind, randomized, controlled clinical trial designed to support FDA marketing approval of the

NICE Specialist comments

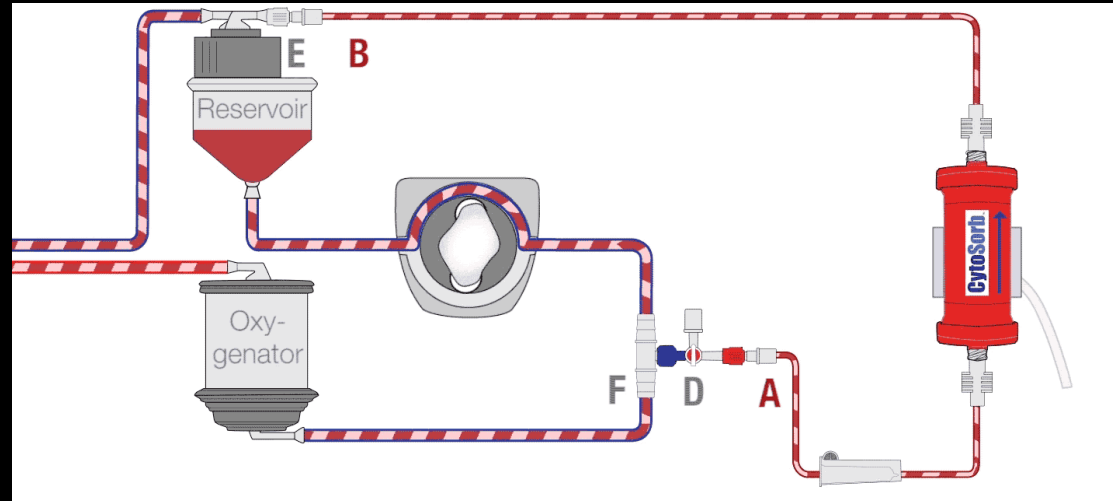
❖ Potential system impact and general comments

- All experts agreed that CytoSorb has the potential to change the current pathway.

❖ Randomised clinical trials are needed to address the uncertainty in the evidence base.

- should ideally include a multi-ethnic population.

MIB IMPLICATIONS



**AVAILABILITY
TO USE IN
THE NHS**

**STAR Trials
NEW
EVIDENCE**

**WIDER
IMPACT
COMPARISON**



❖ “One must be progressive in heart and active in promoting the progressive principles of today, tomorrow and always.

❖ “There is no resting point”

– Charles Lindbergh

An aerial photograph of the Royal Brompton & Harefield Hospital complex, showing various buildings, a central tower, and surrounding greenery. A large, solid red heart is superimposed over the center of the image, containing the text "Thank you!".

Thank you!

