Be Ready.
When Minutes Matter®

Pathogen Reduced Cryoprecipitated Fibrinogen Complex

INTERCEPT® Fibrinogen Complex (IFC)

*INTERCEPT Fibrinogen Complex is available for immediate use for up to 5 days when stored thawed; and when stored frozen requires thawing prior to use.

Pathogen Reduced Cryoprecipitated Fibrinogen Complex

INTERCEPT® Fibrinogen Complex (IFC)

Nadia Keltner, MSc, PhD

Clinical Market Development Director, Cerus

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The INTERCEPT® Fibrinogen Complex Advantage

*INTERCEPT Fibrinogen Complex is available for immediate use for up to 5 days when stored thawed; and when stored frozen requires thawing prior to use.
†Bleeding associated with fibrinogen deficiency
‡Broad spectrum transfusion transmitted infection risk reduction

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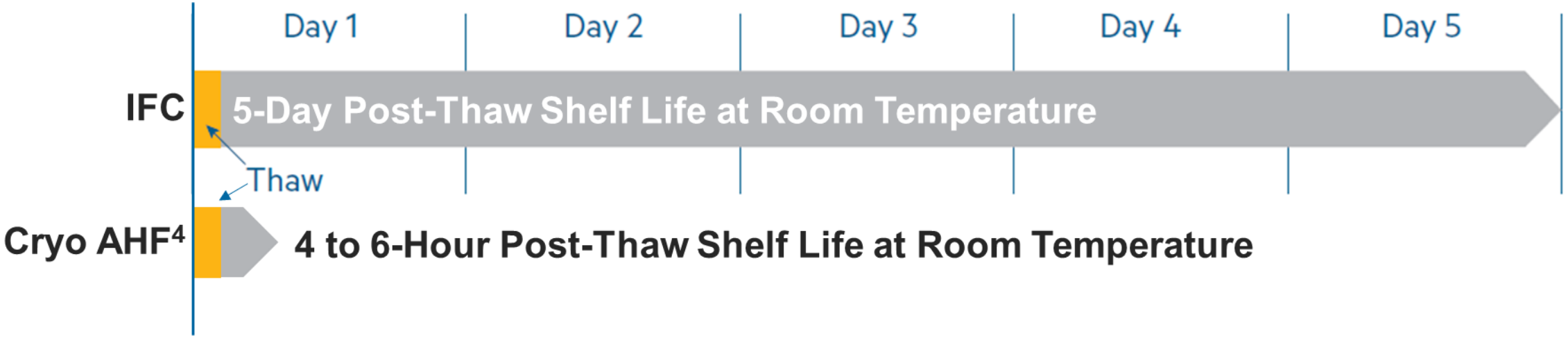
Thawed IFC is Grab and Go with the First Blood Products

- Immediate*, enriched source of key factors in effective hemostasis[1-3]
  - Fibrinogen
  - Factor XIII
  - von Willebrand Factor
  - Other vital clotting proteins



1. Levy JH et al. Transfusion 2014;54:1389-405; quiz 1388. 2. Schroeder V et al. Seminars in Thrombosis and Hemostasis 2016;42(4):422-428. 3. Peyvandi, F. Blood Transfusion 2018;16(4):326-328. 4. AABB. Circular of Information for the Use of Human Blood and Blood Components. Bethesda, MD: AABB; 2024; 2024. AABB.
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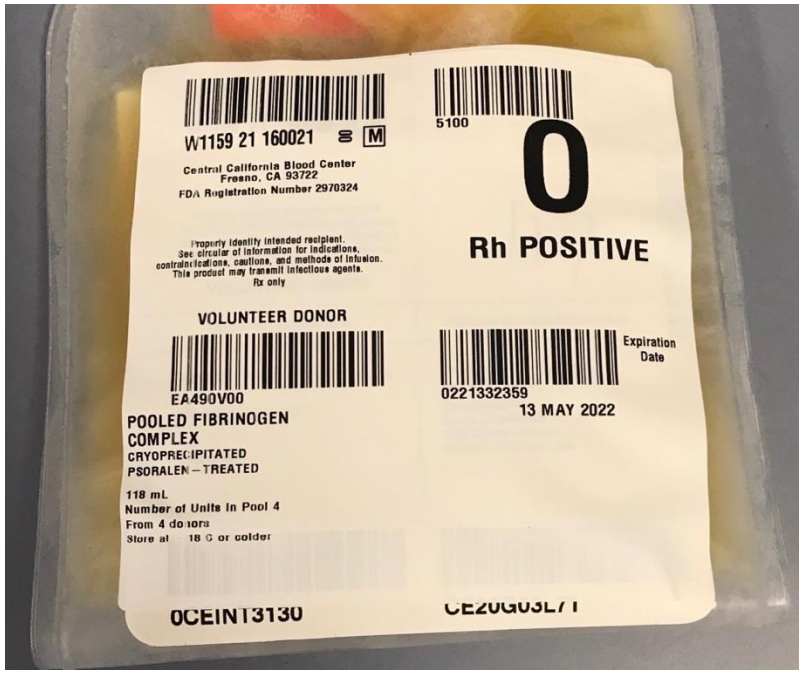
Pathogen Reduced Cryoprecipitated Fibrinogen Complex
Indications for Use

- Treatment and control of bleeding, including massive hemorrhage, associated with fibrinogen deficiency.
- Control of bleeding when recombinant and/or specific virally inactivated preparations of factor XIII or von Willebrand factor (vWF) are not available.
- Second-line therapy for von Willebrand disease (vWD).
- Control of uremic bleeding after other treatment modalities have failed.

Limitations of Use: Pathogen Reduced Cryoprecipitated Fibrinogen Complex should not be used for replacement of factor VIII.

INTERCEPT Fibrinogen Complex (IFC)



1. INTERCEPT Blood System for Cryoprecipitation for the Manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert.

Pathogen Reduced Cryoprecipitated Fibrinogen Complex
Contraindications, Warnings, Precautions

CONTRAINDICATIONS

- Contraindicated for preparation of blood components intended for patients with a history of hypersensitivity reaction to amotosalen or other psoralens.
- Contraindicated for preparation of blood components intended for neonatal patients treated with phototherapy devices that emit a peak energy wavelength less than 425 nm, or have a lower bound of the emission bandwidth <375 nm, due to the potential for erythema resulting from interaction between ultraviolet light and amotosalen.

WARNINGS AND PRECAUTIONS

- Only the INTERCEPT Blood System for Cryoprecipitation is approved for use to produce Pathogen Reduced Cryoprecipitated Fibrinogen Complex.
- For management of patients with vWD or factor XIII deficiency, Pathogen Reduced Cryoprecipitated Fibrinogen Complex should not be used if recombinant or specific virally-inactivated factor preparations are available. In emergent situations, if recombinant or specific virally-inactivated factor preparations are not available, Pathogen Reduced Cryoprecipitated Fibrinogen Complex may be administered.

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1. INTERCEPT Blood System for Cryoprecipitation for the Manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert.

Roman Dudaryk, M.D.

Professor, Clinical Anesthesiology
Director of Quality, Department of Anesthesiology
University of Miami Miller School of Medicine
Jackson Memorial Hospital
Miami, Florida

Bio:

Dr. Roman Dudaryk is the Professor of Anesthesiology and Director of Quality in the Department of Anesthesiology, Perioperative Medicine, and Pain Management at the University of Miami Miller School of Medicine.

Dr. Dudaryk completed a Residency in Anesthesiology at Jackson Memorial Hospital where he served as chief resident, a Fellowship in Critical Care Medicine and Perioperative Echocardiography at Duke University and is board certified in Anesthesiology, Critical Care Medicine, and Perioperative Transesophageal Echocardiography.

Dr. Dudaryk is the author of more than 50 peer-reviewed publications, invited editorials, review articles, book chapters and numerous abstracts at national and international meetings. His personal research interests are trauma-induced coagulopathy, resuscitation, transfusion, viscoelastic monitoring, perioperative anticoagulation management and medical alarms, and lectures nationally on these topics.

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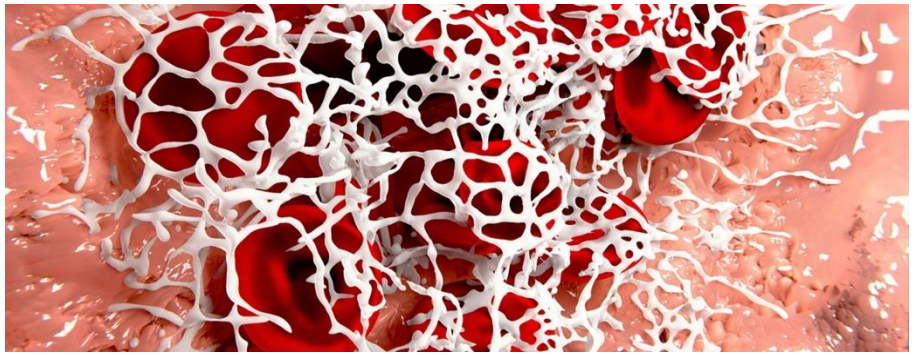
Optimizing Fibrinogen Replacement: Pathogen-Reduced Cryoprecipitated Fibrinogen Complex in Trauma

INTERCEPT® Fibrinogen Complex (IFC)

Roman Dudaryk MD
Professor of Anesthesiology,
Director of Quality
University of Miami/Ryder Trauma Center



Fibrinogen

Most abundant coagulation factor
Clot Mesh

- 1st factor depleted in massive hemorrhage
- Hypofibrinogenemia = AFD (acquired fibrinogen deficiency, < 150 mg/dL, up to 40% of severe traumas)
- Correlation with ISS
- Correction improves survival

Ponschab et al.. Anaesthesia. 2015; 70(5): 528-536.
Spahn et al.,. Crit Care. 2019; 23:98.

Cryostat 2: Caveats and Pitfalls with Cryoprecipitated AHF (Cryo AHF)

JAMA®

QUESTION Does early transfusion of high-dose cryoprecipitate in addition to standard care improve survival in patients with trauma and bleeding who require activation of a major hemorrhage protocol (MHP)?

CONCLUSION The addition of early and empirical high-dose cryoprecipitate to usual care did not improve clinical outcomes in patients with trauma and bleeding.

POPULATION

1251 Men **330** Women

Patients 16 years or older with major trauma hemorrhage in the emergency department

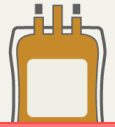
Median age: **39** years

LOCATIONS

26
Major trauma centers in the UK and the US

INTERVENTION

1604 Participants randomized
1531 Participants analyzed



799
Cryoprecipitate
Standard treatment with an additional 3 pools of cryoprecipitate (6-g fibrinogen) as early as possible

805
Standard care
Standard treatment according to the local MHP with a balanced ratio of red blood cells and fresh frozen plasma

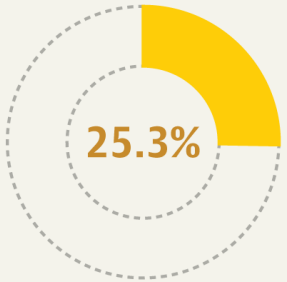
PRIMARY OUTCOME

All-cause mortality at 28 days

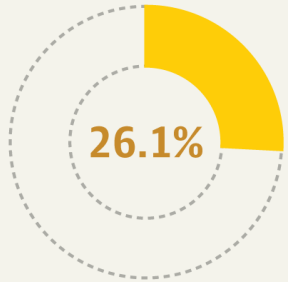
FINDINGS

All-cause mortality at 28 days

Cryoprecipitate
192 of 760 participants

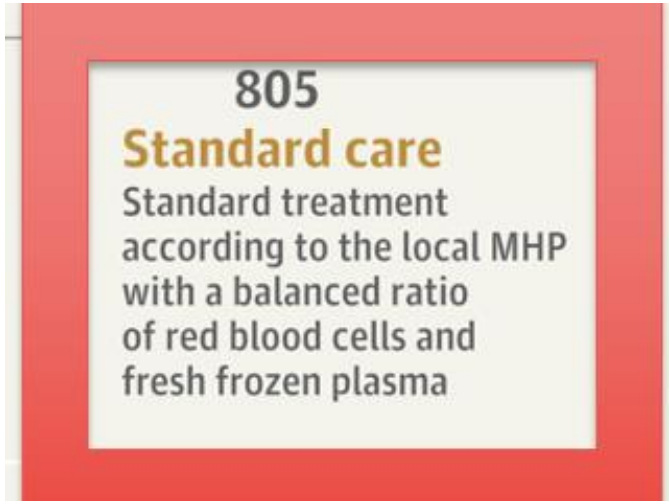


Standard care
201 of 771 participants



There was no improvement in mortality:
Odds ratio, 0.96 (95% CI, 0.75-1.23); *P* = .74

Davenport R, Curry N, Fox EE, et al; for the CRYOSTAT-2 Principal Investigators. Early and empirical high-dose cryoprecipitate for hemorrhage after traumatic injury: the CRYOSTAT-2 randomized clinical trial. *JAMA*. Published online October 12, 2023. doi:10.1001/jama.2023.21019

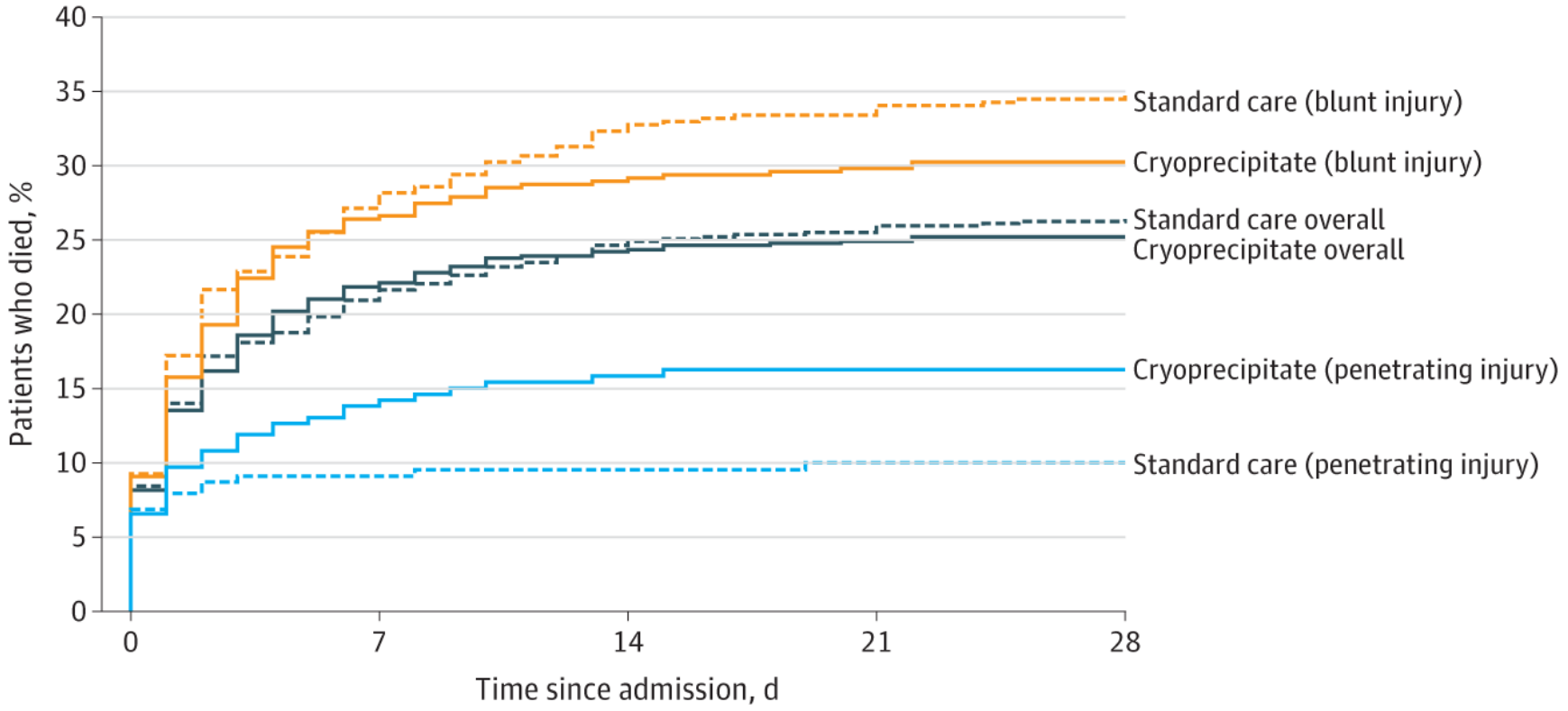


Standard MHP

(Low Dose, Delayed Fibrinogen Replacement)

- 2 pools of cryo AHF (4-g fibrinogen equivalent) in 2nd and subsequent packs.
- **32% Received cryo AHF in Control**
- **85%** Received cryo AHF in **Intervention,** but only **42%** according to protocol
- Median time to transfusion

Mortality by Injury Type



No. of patients at risk

Cryoprecipitate overall	784	567	532	514	498
Standard care overall	795	569	518	501	479
Cryoprecipitate (blunt injury)	495	348	332	323	310
Standard care (blunt injury)	518	353	320	307	289
Cryoprecipitate (penetrating injury)	289	219	200	191	188
Standard care (penetrating injury)	277	216	198	194	190

Role of Fibrinogen in Trauma-Induced Coagulopathy

Jonathan P Meizoso, MD, MSPH, Ernest E Moore, MD, FACS, Fredric M Pieracci, MD, MPH, FACS, Rebecca A Saberi, MD, Arsen Ghasabyan, MPH, James Chandler, BS, Nicholas Namias, MD, MBA, FACS, Angela Sauaia, MD, PhD

Journal of the American College of Surgeons

- 476 patients, highest-level activation
- Median NISS: 25
- 15% with fibrinogen < 150
- 15% mortality
  - 24-hour mortality: 26% (low fibrinogen) vs. 6% (normal)

- Admission fibrinogen level predictive of MT

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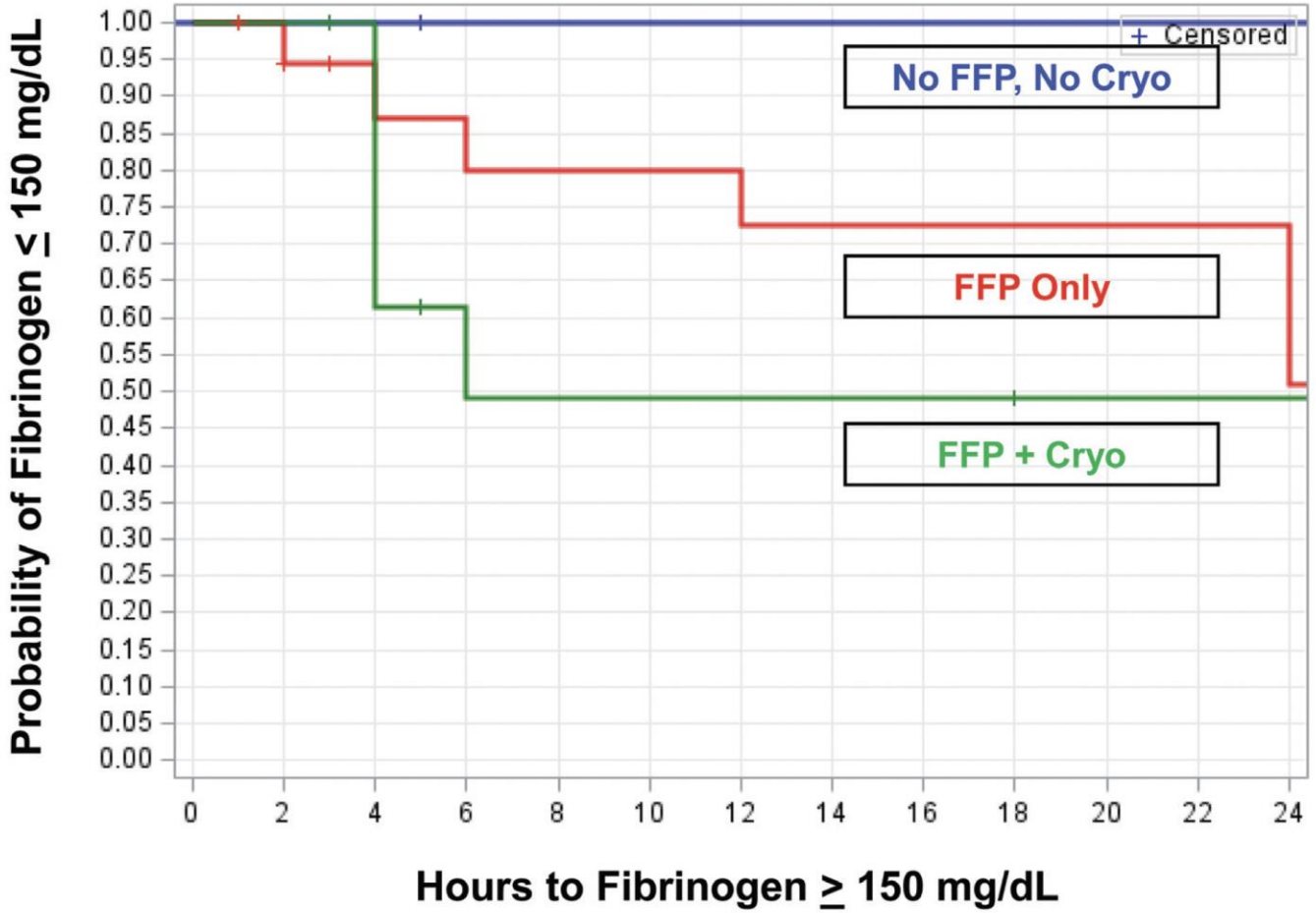


Cryoprecipitate (cryo AHF) offered fastest time to correction of low fibrinogen

Pre-IFC MHP

Cryo AHF delayed or not given

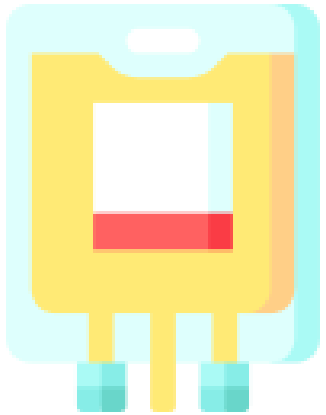
- Protocol: 1 pulled unit of Cryo AHF with 3rd round
- REALITY: between 3rd and 6th round (>2 hrs. since admission)

Post-IFC MHP

IFC administered at MTP initiation

- 2 FC10 doses (~1.5 grams of fibrinogen)
- 2nd round of MTP

** 1st Round of MTP – 2 Units Whole Blood*



INTERCEPT Fibrinogen Complex

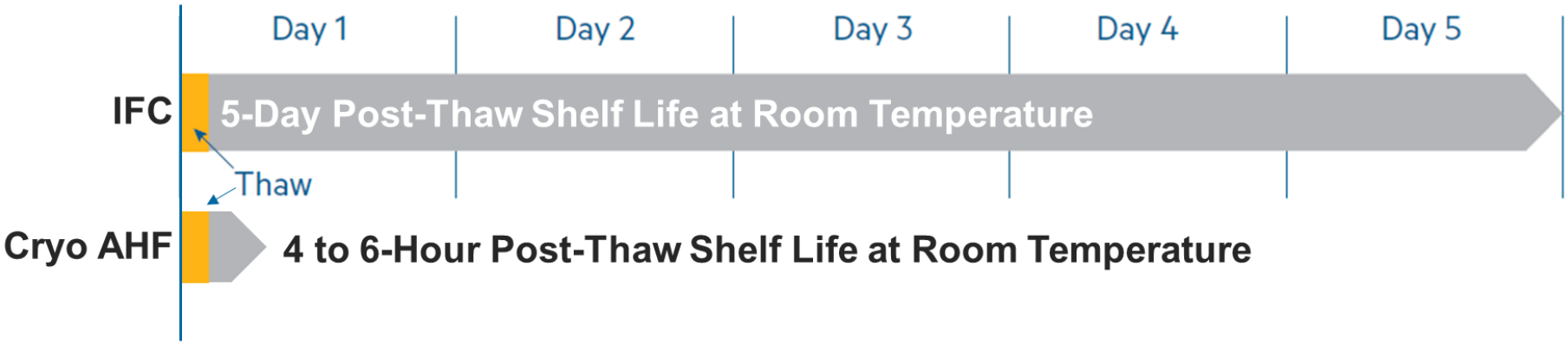
Pathogen Reduced Cryoprecipitated Fibrinogen Complex

PRCFC

- Fibrinogen
- Factor XIII
- Von Willebrand Factor
- Other proteins

INTERCEPT: Immediate* availability of first and additional doses

PRODUCT	IMMEDIATE AVAILABILITY	ROUND 1	ROUND 2	ROUND 3
INTERCEPT® Fibrinogen Complex	Room Temp ≤ 5 Days*	✓	✓	✓
— OR —				
Cryoprecipitated AHF[2]	Room Temp ≤ 4-6 Hours	*Availability delayed due to time to thaw, established into later rounds of MTPs[1]*		✓



1. Holcomb JB, et al. The Journal of Trauma and Acute Care Surgery 2013;75:S31-S39. 2. AABB. Circular of Information for the Use of Human Blood and Blood Components. Bethesda, MD: AABB; 2024.
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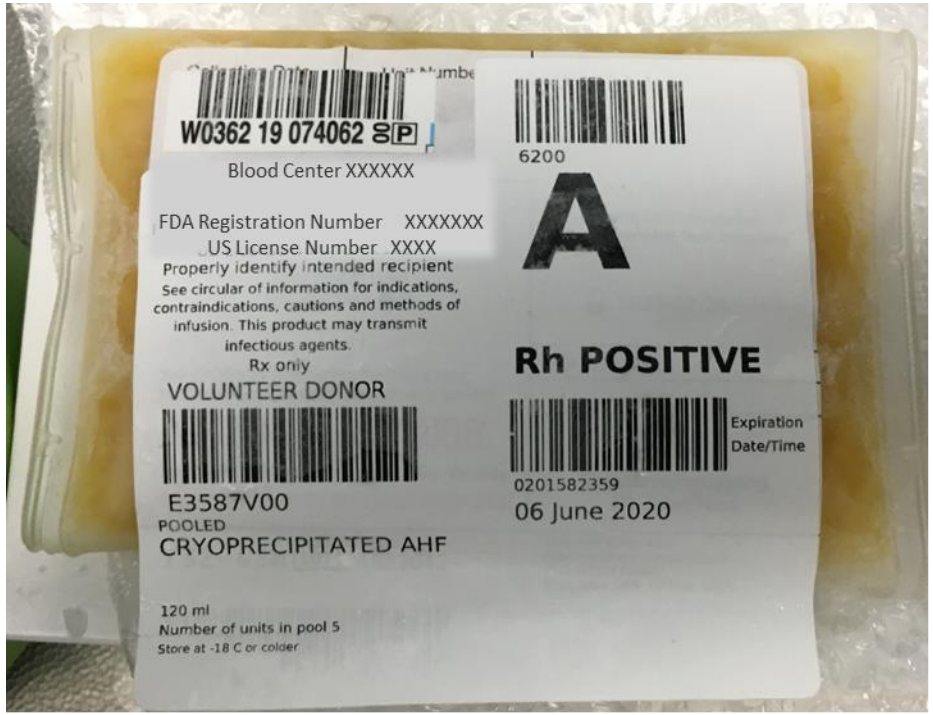
Pathogen Reduced Cryoprecipitated Fibrinogen Complex Doses

Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT Fibrinogen Complex, IFC)				Approximate Fibrinogen Equivalency	
Product Code	Mean (SD) Fibrinogen (mg)	Whole Blood Inputs (Donors)	Avg Volume (ml)	Cryo AHF	Fibrinogen Concentrate
FC10	**740** (166)	2	60	2x single donor	1 vial
FC15	**1,556** (248)	4	120	5-pool	1.5 vials

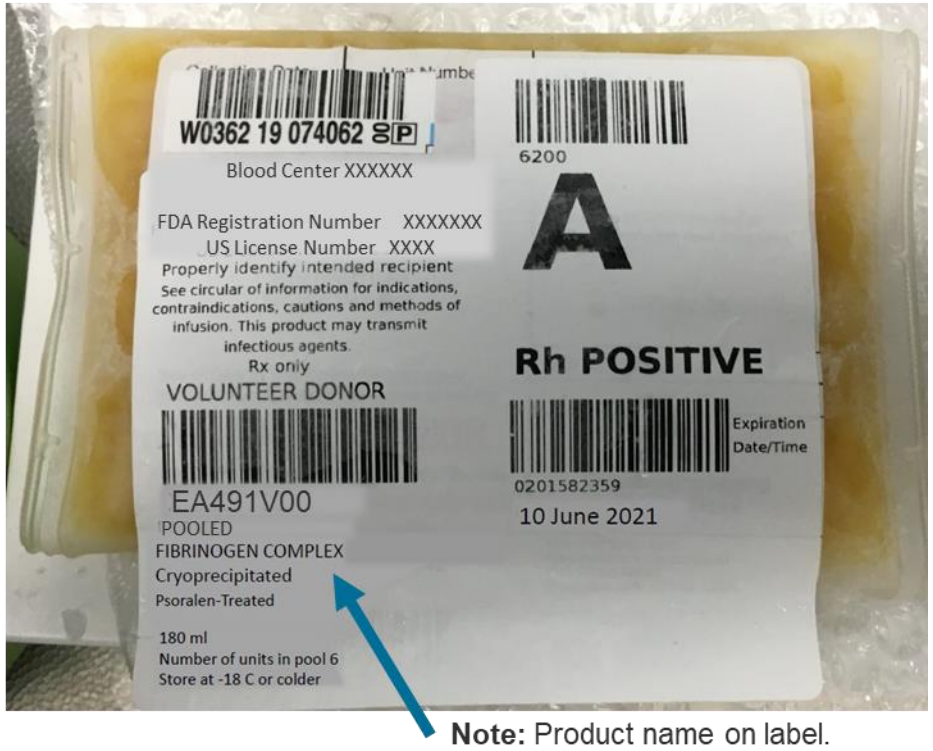
INTERCEPT Blood System for Cryoprecipitation for the Manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex Package Insert.

How does it look?

Cryoprecipitated AHF Label



INTERCEPT Fibrinogen Complex Label



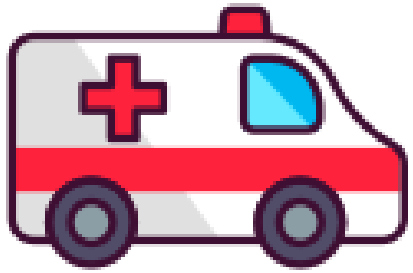
Note: Product name on label.

3.7%*

Wastage rate post-IFC implementation of dual inventory IFC and cryo AHF

Goal < 12%
Historical average 20% cryo AHF

*Institutional data

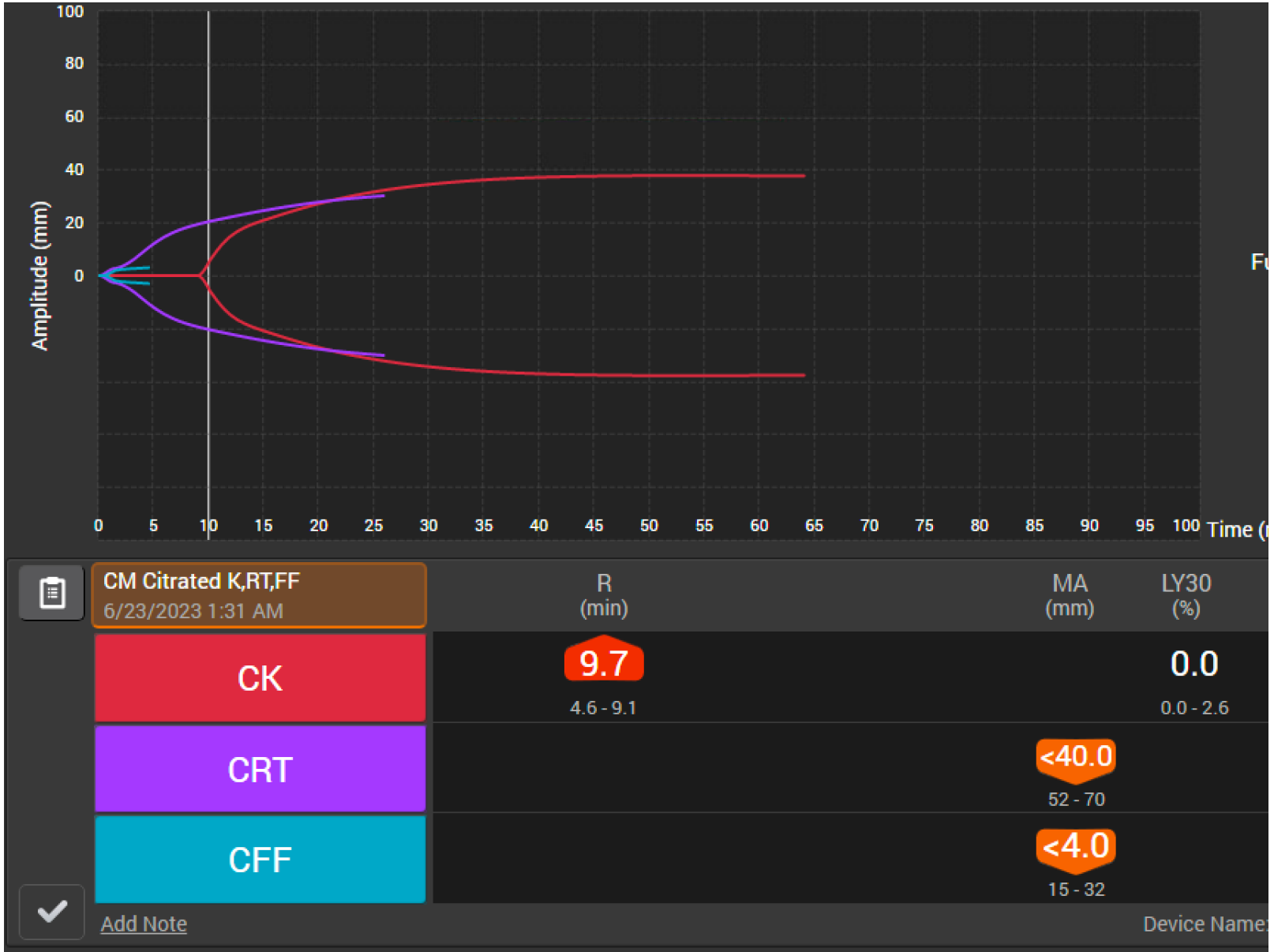


MVC Transfer

Outside Hospital

- 57 y.o.
- BP 110/45
- HR 124
- RA, mild distress
- **Getting PRBC and IVF started during transfer**
- Positive FAST

Low Fibrinogen: Citrated Functional Fibrinogen <4.0 mm on CFF MA



MTP

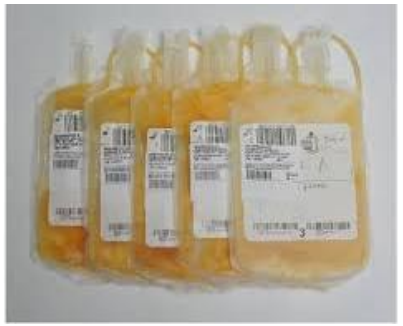
Grade IV liver lac

- 2 units of Whole Blood
- 2 Rounds of MTP
- 2 doses of PRC :
  1st part of MTP
  2nd guided by TEG

CFF MA of 12 mm = 150 mg/dl

CFF MA vs Fibrinogen Level by Clauss method

Anesth Analg. 2020; 130(3):644-653



Most Frequent Abnormality in Hemostatic Resuscitation: Low Fibrinogen[1]

1:1:1 ratios

- Before hemostatic resuscitation: 8-20% (consumption and dilution components)
- Hemostatic resuscitation era: 7-15% (less dilution)

1. Hagemo JS, et al. Critical care. 2014;18(2):R52.

Anaesthesia 2015, 70, 528–536 doi:10.1111/anae.13067

Original Article

Haemostatic profile of reconstituted blood in a proposed 1:1:1 ratio of packed red blood cells, platelet concentrate and four different plasma preparations

M. Ponschab,[1] H. Schöchl,[2,3] C. Gabriel,[4] S. Süssner,[5] J. Cadamuro,[6] E. Haschke-Becher,[7] J. Gratz,[8] J. Zipperle,[1] H. Redl[9] and C. J. Schlimp[2]

1.5– 1.9 g/l

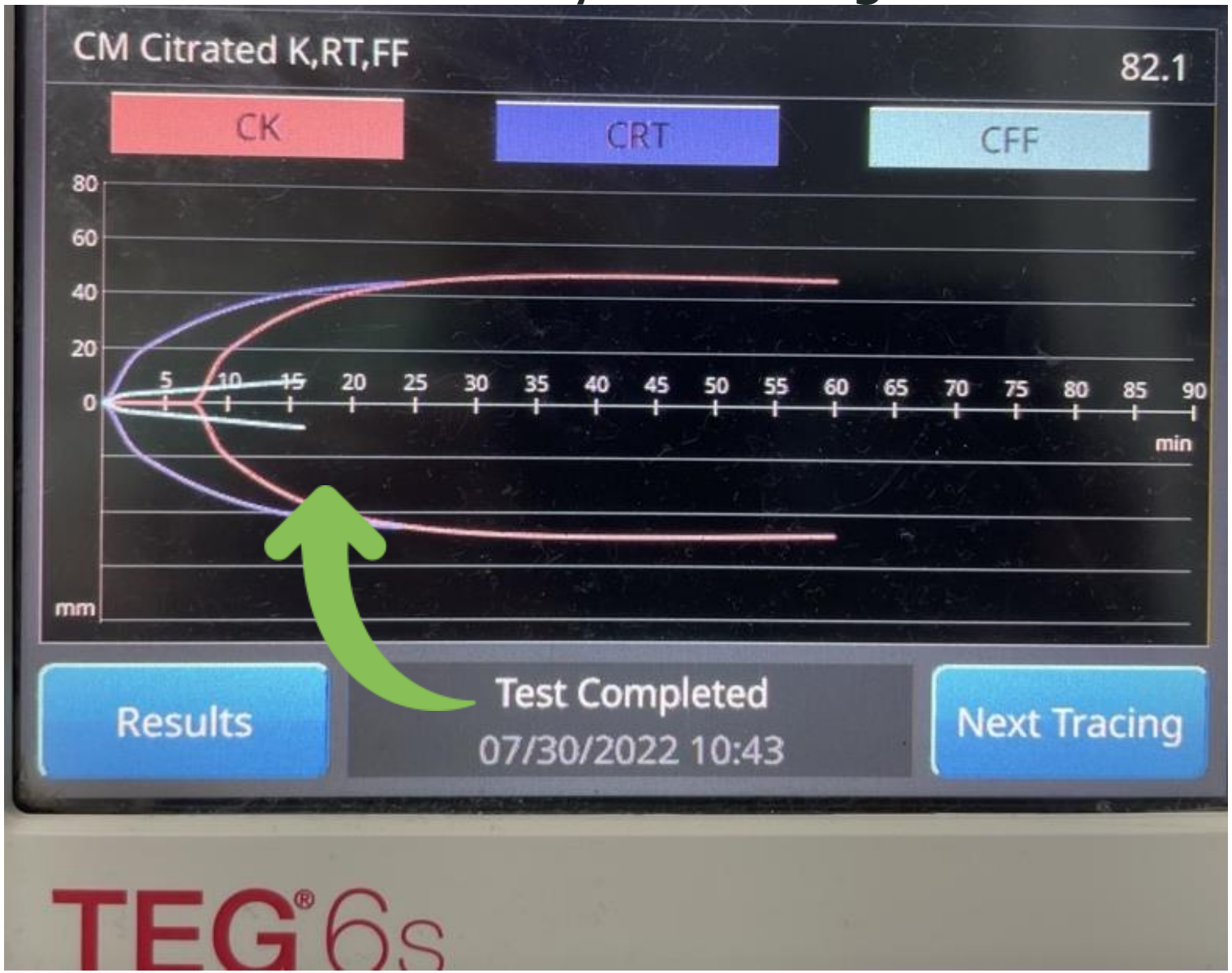
Fibrinogen concentration in reconstituted blood (1:1:1)

Motor Vehicle Collision (MVC)

Splenectomy

- 42 y.o. MVC
- BP 82/40
- HR 133
- OR
- 2 Rounds MTP
  8 PRBC
  8 FFP
- Stabilized

Most Common Deficiency… Fibrinogen



Institutional IFC Data: CAT Positive Traumas Patients

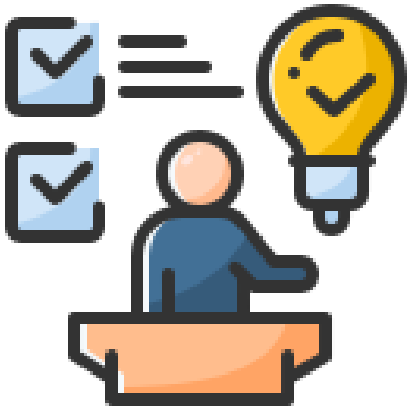
CAT: Critical Administration Threshold

- Inclusion:
  CAT + Patients within 4 hrs.
  CAT: 2 of LTOWB or 3 Units of PRBC in 1 hr.
- Controlled for :
  Age
  Gender
  Mechanism
  SBP
  HR
  GCS
  Base deficit
  LTOWB use

Comparison of Key Outcomes in CAT-Positive Trauma Patients Within the First 4 Hours Before and After Implementation of IFC*

Outcome	Pre IFC	Post IFC	p-value
Patients receiving any cryoprecipitate	21.9% (32)	23.1% (31)	0.808
Volume of cryoprecipitate	300 [250-500]	250 [147-583]	0.171
Patients receiving any whole blood	38.4% (56)	70.1% (94)	**<0.001**
Total blood product volume	**2357 [1500-4103.75]**	**1952 [1242.5-2719.75]**	**0.004**
Mortality	**42.5% (62)**	**33.6% (45)**	**0.126**
VTE	6.5% (10)	11.2% (15)	0.203
AKI	4.8% (7)	5.2% (7)	0.869

CAT: Critical Administration Threshold(>3 U PRBC or 2 units of LWOB in < 1 hr.)
Total N of patients: 280 (146 pre, 134 post)
* Unpublished data



Conclusions

IFC for Acquired Fibrinogen Deficiency (AFD) in Trauma

- AFD is common coagulation problem in the era of hemostatic resuscitation
- IFC enables rapid fibrinogen supplementation of AFD
- IFC facilitates early fibrinogen transfusion
- Reduction in wastage
- IFC use may be associated with decreased overall blood product requirements*

*IFC has not been evaluated in randomized clinical trial