
Goya (1799)

# HLA is not just for the transplanter: Platelet transfusions and refractoriness

**IDRC 2024**

**Dr. Matthew Seftel**
Canadian Blood Services
University of British Columbia, Canada

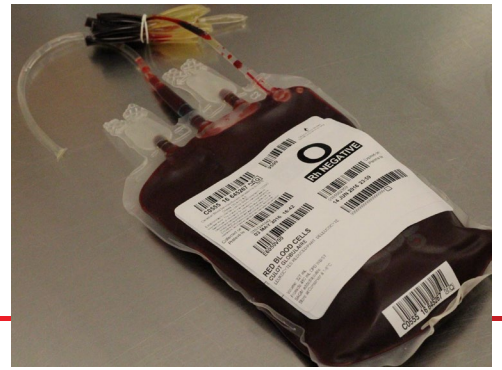
Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

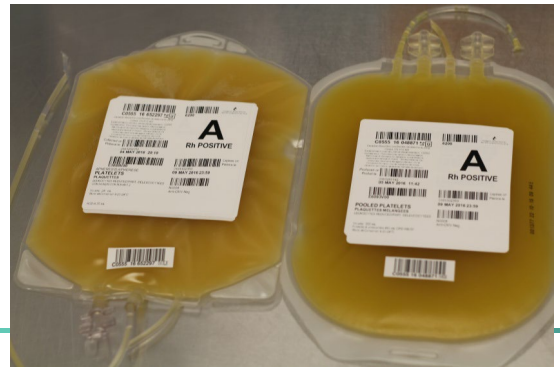
# Disclosures

Employee Canadian Blood Services

# Special transfusion risks to consider in HCT

- Iron overload
- ABO incompatibility
- TACO
- Platelet refractoriness
- TA-GVHD
- Infection



# Objectives for today

1. Review trends in platelet transfusion practice

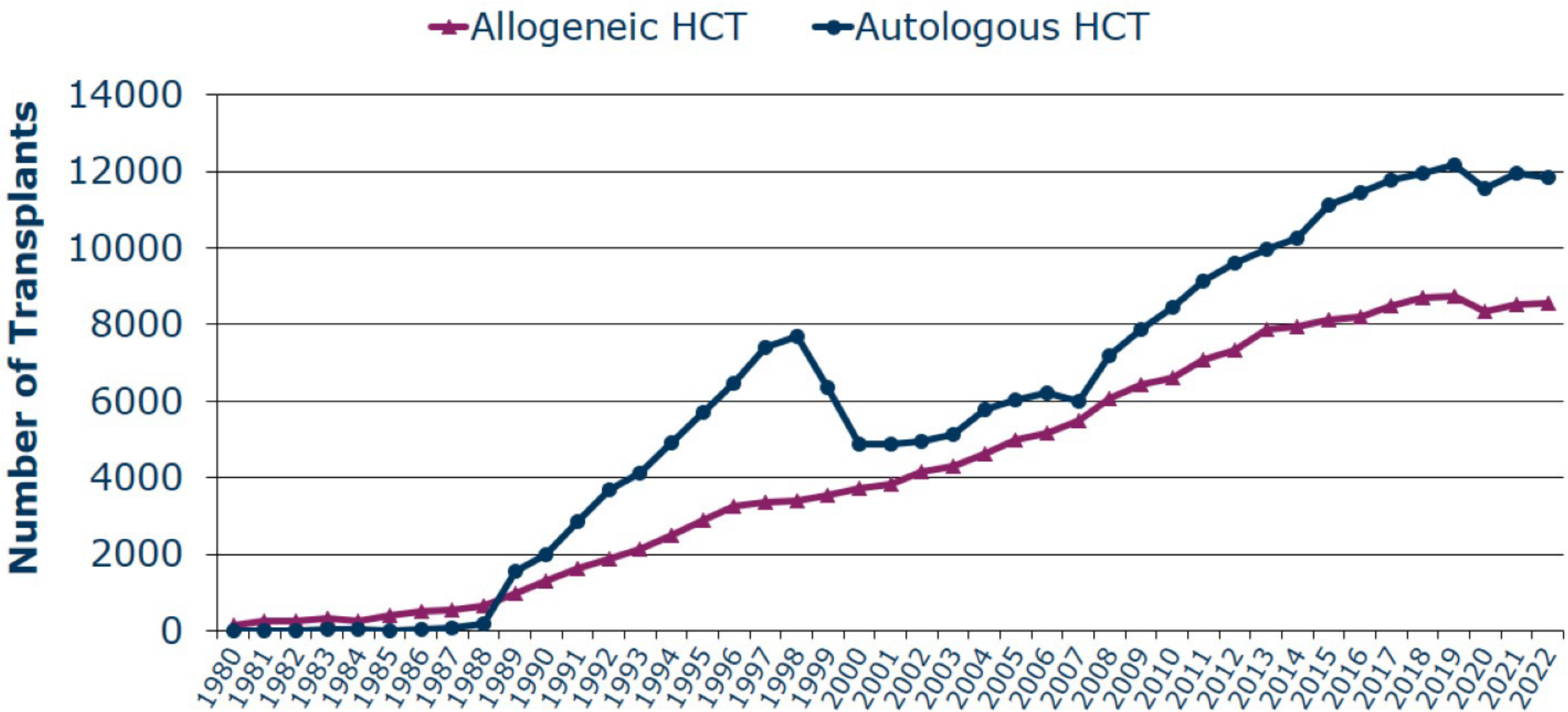
2. Review causes and patterns of platelet transfusion refractoriness

3. Outline diagnosis and management of PLT refractoriness caused by alloimmunization

# Objectives for today

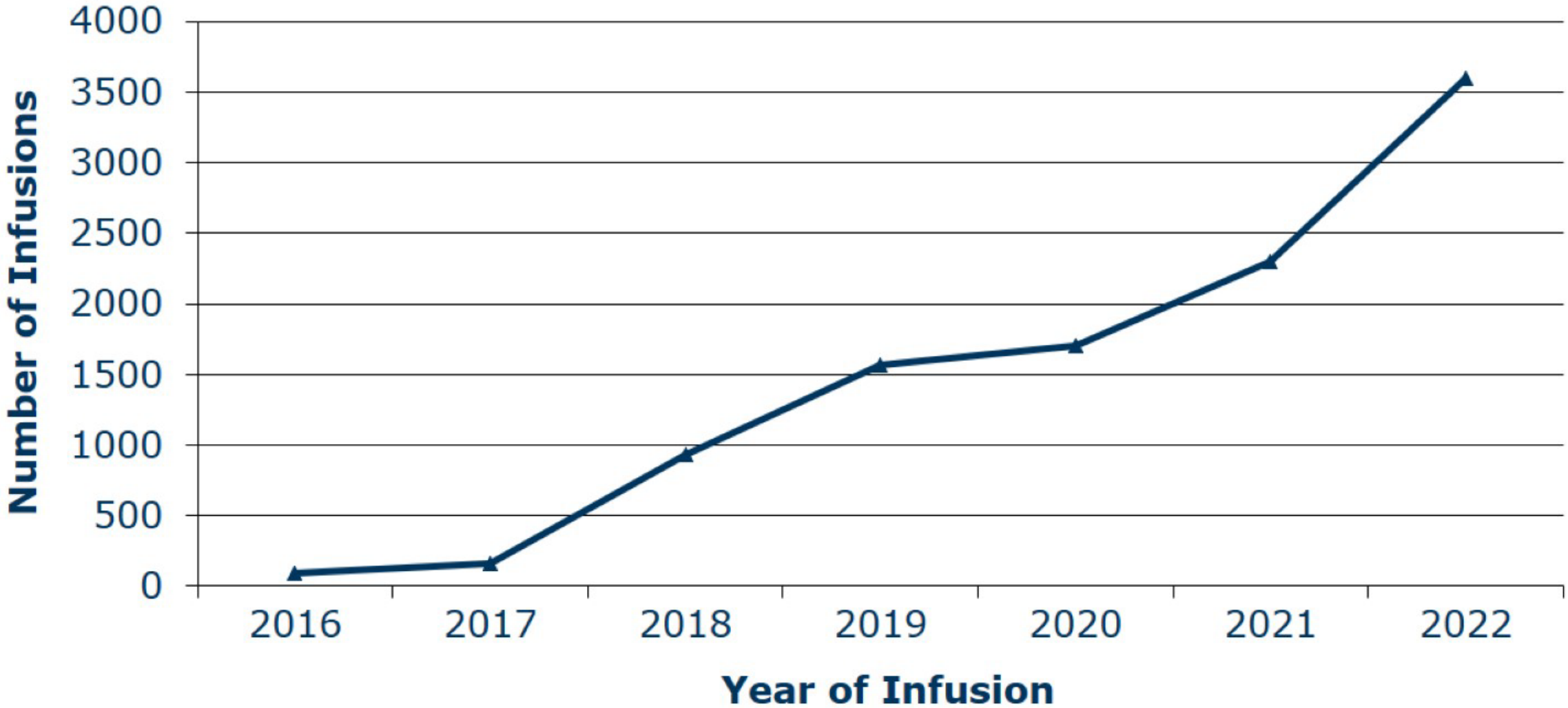
1. **Review trends in platelet transfusion practice**
2. Review causes and patterns of platelet transfusion refractoriness
3. Outline diagnosis and management of PLT refractoriness caused by alloimmunization

# *Number of 1st HCTs Reported to CIBMTR in the US*




CIBMTR®
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

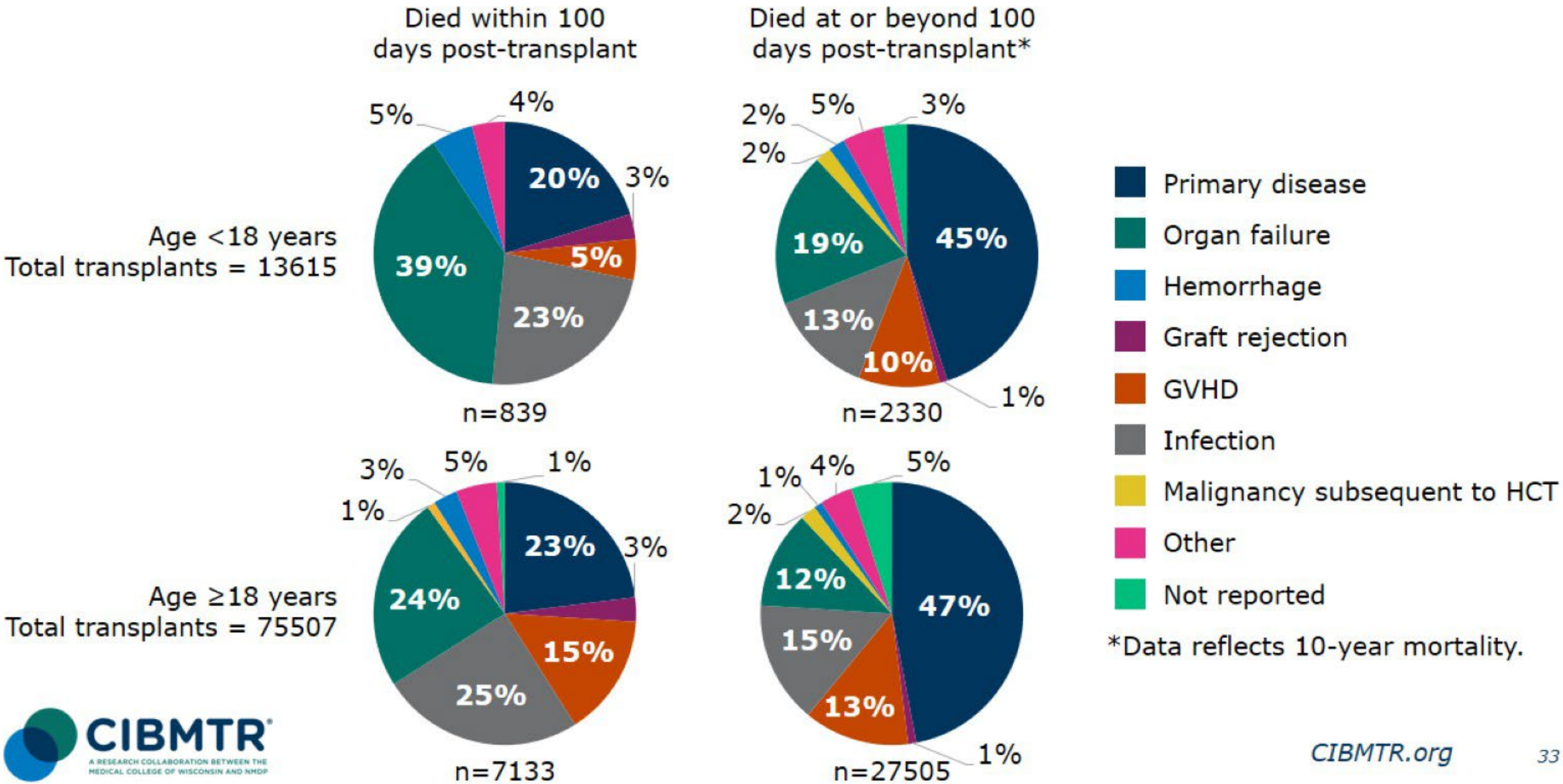
# *Number of 1st CAR-T Infusions Reported to CIBMTR in the US*




CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

Abbreviations: CAR-T, chimeric antigen receptor T-cell

# *Causes of Death after Allogeneic HCTs in the US, 2012-2022*




CIBMTR
A RESEARCH COLLABORATION BETWEEN THE MEDICAL COLLEGE OF WISCONSIN AND NMDP

# What is the typical threshold for prophylactic platelet T/F in stable HM/HCT pts?

A. $<10x10^9/L$
B. $<10x10^9/L$ & tranexamic acid
C. $<20x10^9/L$
D. T/F is not required prophylactically

# Prophylactic plts at <10K vs. no prophylaxis in HM/HCT

| Outcome | No Prophylaxis (N=301) | Prophylaxis (N=299) | No Prophylaxis vs. Prophylaxis | P Value |
|---|---|---|---|---|
| **Primary end point** | | | | |
| WHO grade 2, 3, or 4 bleeding — no. (%) | 151 (50) | 128 (43) | 8.4 (1.7 to 15.2)†‡ | 0.06§ |

Stanworth S et al. NEJM 2013

# Prophylactic plts at <10K vs. no prophylaxis in HM/HCT

| Outcome | No Prophylaxis (N=301) | Prophylaxis (N=299) | No Prophylaxis vs. Prophylaxis | P Value |
|---|---|---|---|---|
| **Primary end point** | | | | |
| WHO grade 2, 3, or 4 bleeding — no. (%) | 151 (50) | 128 (43) | 8.4 (1.7 to 15.2)†‡ | 0.06§ |
| Autologous stem-cell transplantation | 99/210 (47) | 95/210 (45) | 2.3 (–5.7 to 10.3)† | |
| Chemotherapy | 52/90 (58) | 33/88 (38) | 20.0 (7.9 to 32.2)† | 0.04§§ |

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Stanworth S et al. NEJM 2013

# Prophylactic PLTS vs no PLTS *with TXA* in autoHCT

ClinicalTrials.gov

Find Studies ▾ About Studies ▾ Submit Studies ▾ Resources ▾ About Sit

Home > Search Results > Study Record Detail

**Platelet Transfusions in Hematopoietic Stem Cell Transplantation (The PATH III Trial) (PATH)**

ClinicalTrials.gov Identifier: NCT04448184

# Prophylactic TXA to reduce bleeding & T/F in HCT/HM pts?

| | TXA | Placebo | Estimate | 95%CI | P-value |
|---|---|---|---|---|---|
| N | 165 | 165 | | | |
| **Primary Endpoint:** | | | | | |
| Any Grade 2+ Bleed[a] - n/N (%) | 73/145 (50.3) | 78/144 (54.2) | OR=0.83[b] | (0.50, 1.34)[b] | 0.44[b] |
| **Secondary Endpoints:** | | | | | |
| Platelet transfusions - Mean (SD) | 7.7 (8.7) | 7.6 (10.1) | MD=0.07[b] | (-1.90, 2.04)[b] | 0.95[b] |
| Days without Grade 2+ Bleed[c] - Mean (SD) [N] | 28.1 (3.7) [136] | 27.7 (4.7) [132] | MD=0.79[b] | (-0.40, 1.98)[b] | 0.19[b] |

Gernsheimer T et al. Blood 2022

# Prophylactic TXA to reduce bleeding & T/F in BMT/HM pts

**Table 3:** Safety endpoints

| | TXA | Placebo |
|---|---|---|
| N | 163 | 163 |
| Line occlusions | 27 (16.6) | 11 (6.7) |
| Thrombotic events | 6 (3.7) | 9 (5.5) |

Gernsheimer T et al. Blood 2022

# What is the typical threshold for prophylactic platelet T/F in stable pts with HM/HCT

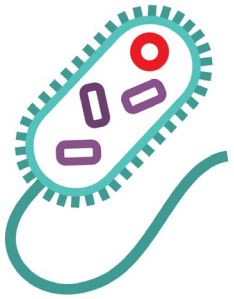
A. <u><$10x10^9$/L</u>
B. <$10x10^9$/L and tranexamic acid
C. <$20x10^9$/L
D. Plt T/F is not required prophylactically

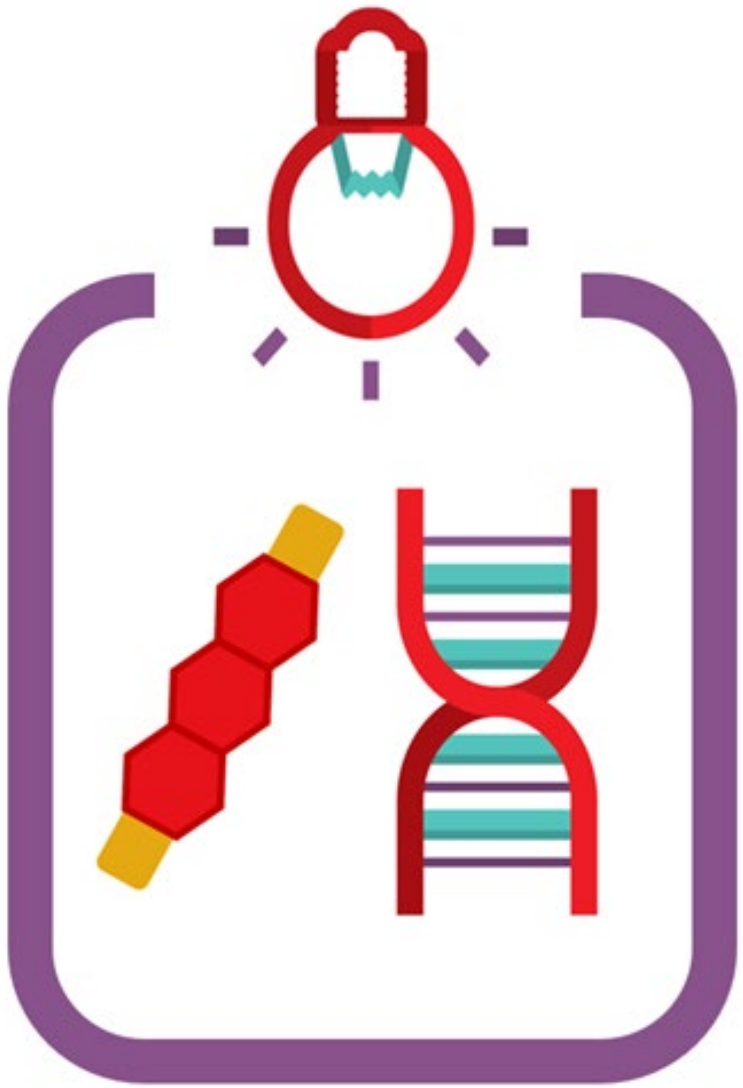
# What is the most common cause of transfusion-transmitted infection?

A. HIV
B. Staphylococcus species
C. Hepatitis C
D. Malaria

# Bacterial contamination of platelet components

- Source: Bacteria from donor skin or blood stream
- Plts stored at room temp - ideal growth medium
- Bacterial sepsis ~1:125,000 of transfused platelet concentrates.



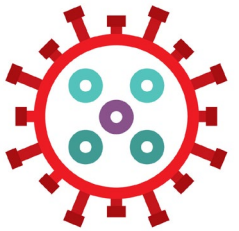


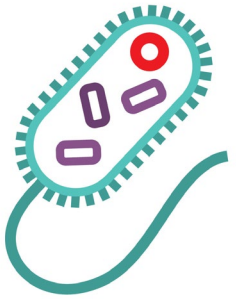
# Pathogen inactivation technology with Amotosalen (Intercept) technology

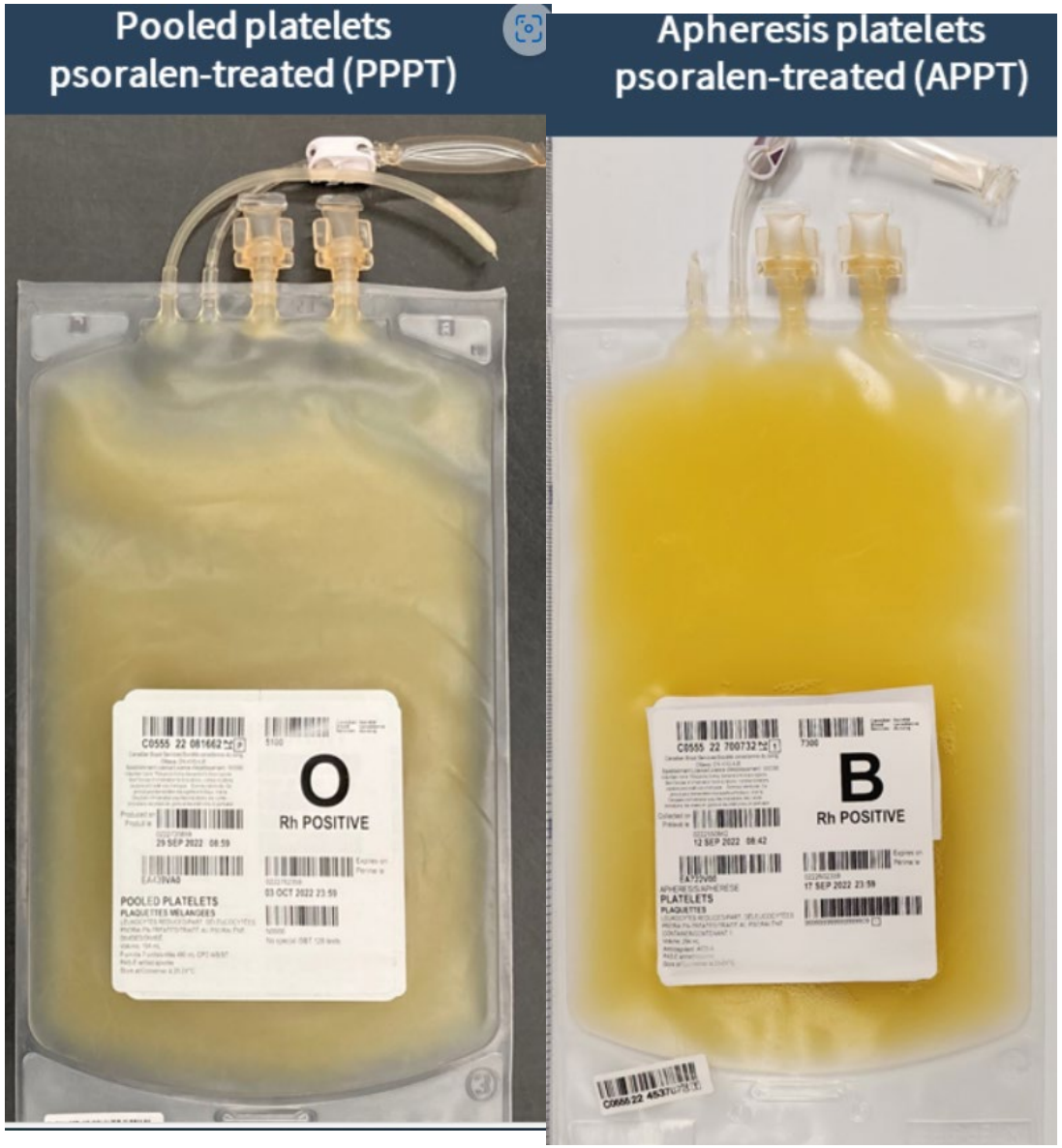
# Pathogen inactivation with Amotosalen/UVA

Additional layer of safety against:

- Viruses
- Bacteria (including spirochetes)
- Protozoa
- Leukocytes - can no longer replicate and produce cytokines








# Pathogen inactivation technology with Amotosalen (Intercept) technology

# Platelet components at CBS

| | Existing platelet components in plasma (prior to 2022) | | New platelet components in PAS-E (as of 2022) | | |
|---|---|---|---|---|---|
| **Component characteristic** | **Untreated pooled platelet** | **Untreated apheresis platelet** | **Untreated apheresis platelet in PAS-E** | **Pooled platelet psoralen-treated (PPPT)** | **Apheresis platelet psoralen-treated (APPT)** |
| | **Untreated (not pathogen-reduced)** | | | **Pathogen-reduced** | |
| Mean unit volume (mL) | 317 | 223 | 269 | 184 | 277 |
| Number of donors in component | 4 | 1 | 1 | 7‡ | 1 |
| Mean plasma volume (mL) | 317 (approximately 20 mL from each of 3 donors + 257 mL plasma from one male donor) | 223 | 113 | 75 (approximately 11 mL per donor) | 116 |
| Approximate platelet yield (x$10^9$ platelets per unit) | 339 | 333 | 279 | 251 | 252 |

Canadian Blood Services — BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Blais-Normandin I et al. CBS Prof Edu 2023

# Q2. What is the most common cause of transfusion-transmitted infection?

A. HIV
B. Staphylococcus species
C. Hepatitis C
D. Malaria

# Objectives for today

1. Review trends in platelet transfusion practice

2. **Review causes and patterns of platelet transfusion refractoriness**

3. Outline diagnosis and management of PLT refractoriness caused by alloimmunization

# What is PLT transfusion refractoriness?

- PLT count ideally ~10- 60 mins after PLT transfusion
  - In a clinically stable pt, increment after 1 dose ~20-40 x $10^9$/L

- **Refractoriness:** Consistently inadequate response to platelet transfusion
  - <5-10x$10^9$/L after 2 consecutive transfusions
  - 1hr CCI <5000-7500 after 2 consecutive transfusions

$$\text{CCI} = \frac{\text{post PLT} - \text{pre-PLT count } (\times 10^9) \times \text{BSA}(m^2)}{\text{PLT dose } (\times 10^{11})}$$

# Causes of PLT refractoriness

| Non-Immune (~80%) | Immune (~20%) |
|---|---|
| Fever, infection, or sepsis | Class I HLA antibodies* |
| Bleeding | HPA antibodies |
| Accelerated platelet consumption (DIC, MAHA) | ABO antibodies |
| Drugs (Ampho, Vanco, ATG, Foscarnet, CAR-T) | Antibodies against drug–platelet glycoprotein complex |
| Splenic Sequestration | Old/poorly stored platelets, small dose |

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Cohn C, ASH Ed 2020; Song X et al, Int J Hematol 2023; *Seftel MD et al, Blood 2004

# Objectives for today

1. Review trends in platelet transfusion practice

2. Review causes and patterns of platelet transfusion refractoriness

3. **Outline diagnosis and management of PLT refractoriness caused by alloimmunization**

blood®

ISSUES FIRST EDITION ABSTRACTS COLLECTIONS AUTH

TRANSFUSION MEDICINE | JANUARY 1, 2004

# Universal prestorage leukoreduction in Canada decreases platelet alloimmunization and refractoriness

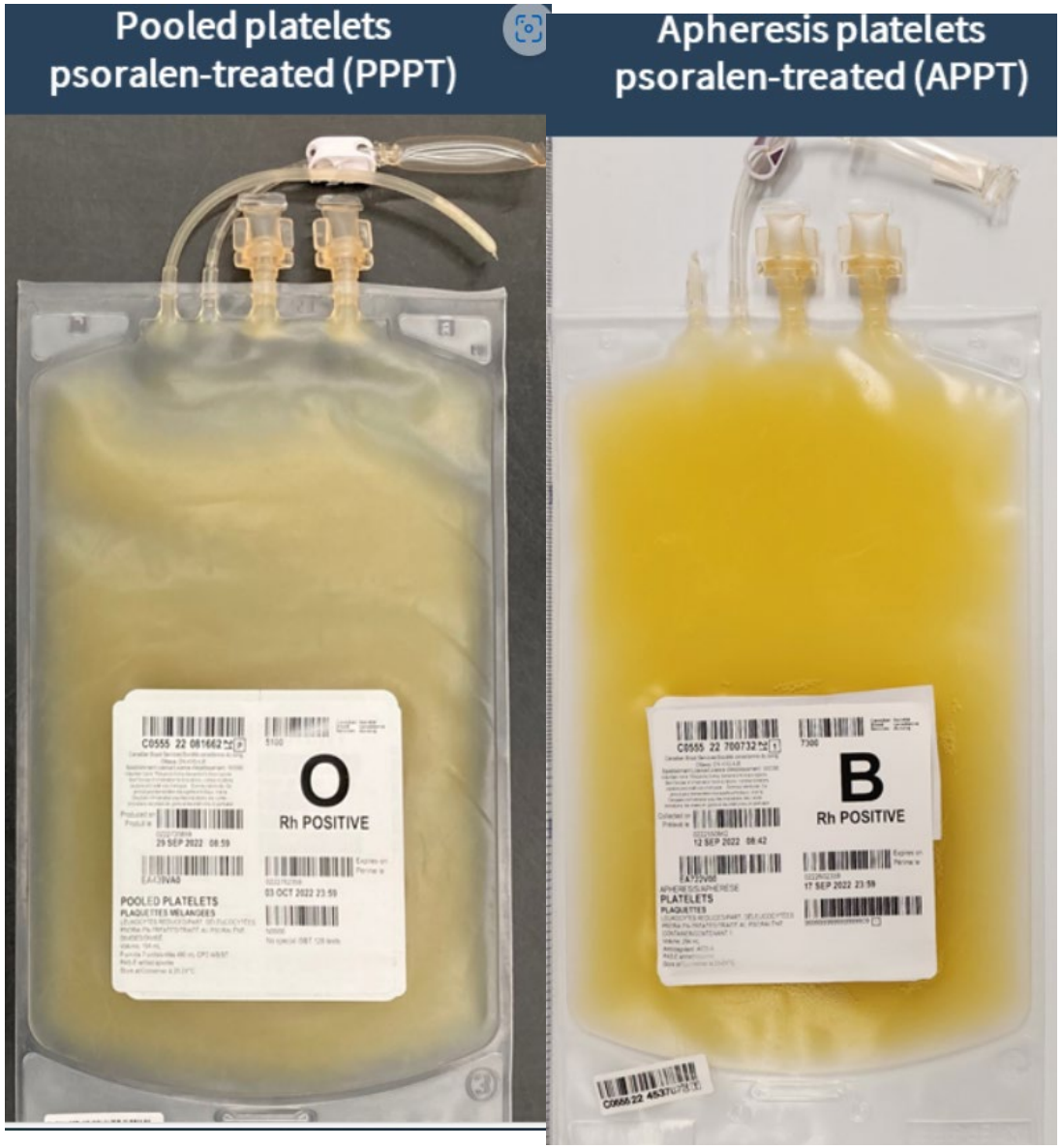
Clinical Trials & Observations

Matthew D. Seftel, Gershon H. Growe, Tanya Petraszko, W. Barrett Benny, Alan Le, Chao-Yong Lee, John J. Spinelli, Heather J. Sutherland, Peter Tsang, Donna E. Hogge



*Blood* (2004) 103 (1): 333–339.

**HLA alloimmune refractoriness: 14% pre to 4% post leukoreduction**



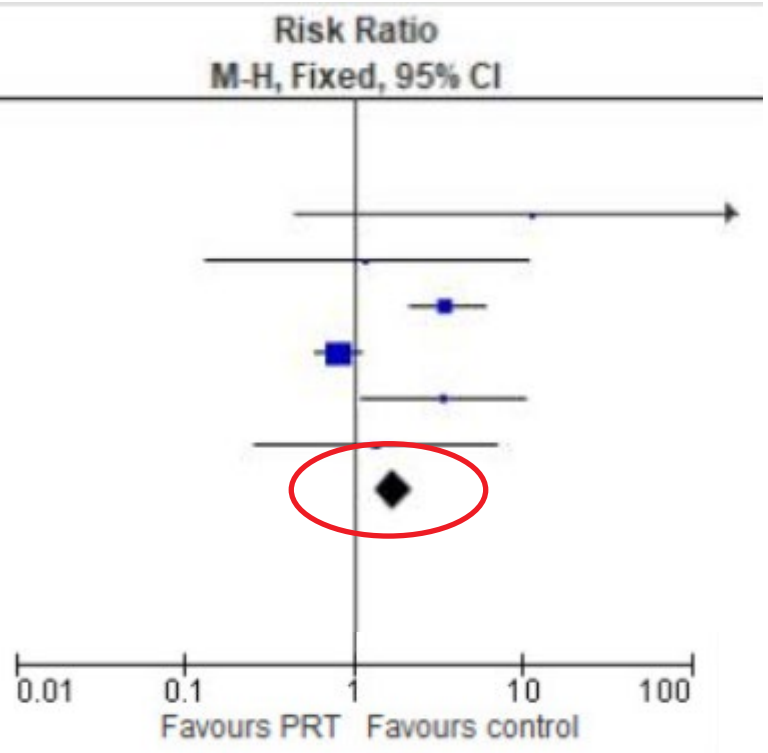

# Pathogen inactivation technology and HLA alloiimunization

# PLT alloimmune refractoriness with Intercept PRT vs controls

| Study or Subgroup | PRT Events | PRT Total | Control Events | Control Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| **1.14.1 intercept vs controls** | | | | | | |
| Agliastro 2006 | 0 | 9 | 0 | 11 | | Not estimable |
| Janetzko 2005 | 4 | 22 | 0 | 21 | 0.4% | 8.61 [0.49, 150.72] |
| Kerkhoffs 2010 | 2 | 85 | 2 | 99 | 1.4% | 1.16 [0.17, 8.09] |
| Mc Cullough 2004 | 68 | 318 | 23 | 327 | 17.4% | 3.04 [1.94, 4.75] |
| Norris-intercept | 46 | 93 | 51 | 86 | 40.5% | 0.83 [0.64, 1.09] |
| Rebulla-Intercept | 15 | 109 | 5 | 107 | 3.9% | 2.94 [1.11, 7.82] |
| Van Rhenen 2003 | 4 | 52 | 3 | 51 | 2.3% | 1.31 [0.31, 5.55] |
| **Subtotal (95% CI)** | | **688** | | **702** | **65.9%** | **1.61 [1.28, 2.02]** |
| Total events | 139 | | 84 | | | |

Heterogeneity: Chi² = 33.52, df = 5 (P < 0.00001); I² = 85%

Test for overall effect: Z = 4.11 (P < 0.0001)



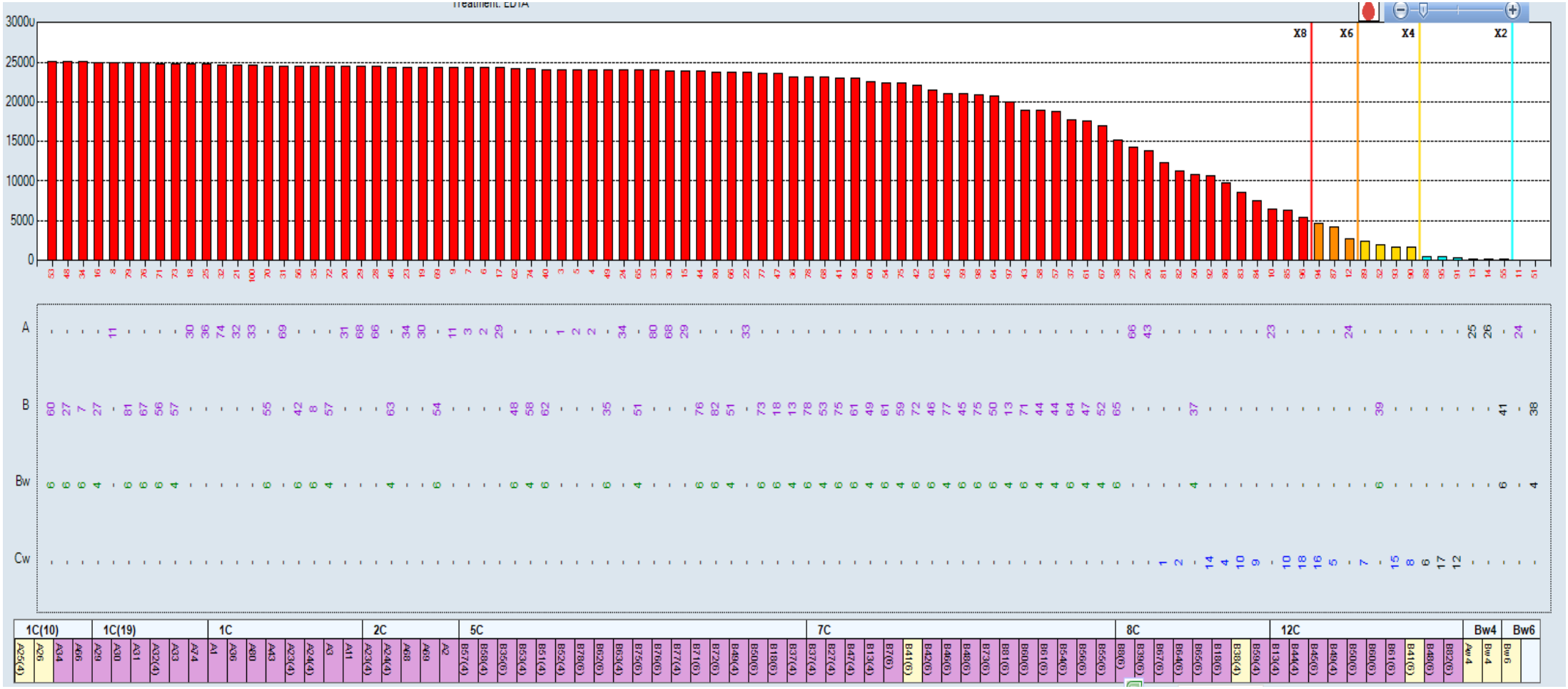

Pati I et al. Pathogens 2022

# How to diagnose immune platelet refractoriness?

- **HLA antibodies?**
- **HPA antibodies?**

- HLA antibody screen
- HPA antibody screen

# HLA Antibody Analysis – Fusion (One Lambda)



# Example of Results

## HLA Class I antibodies detected by Luminex

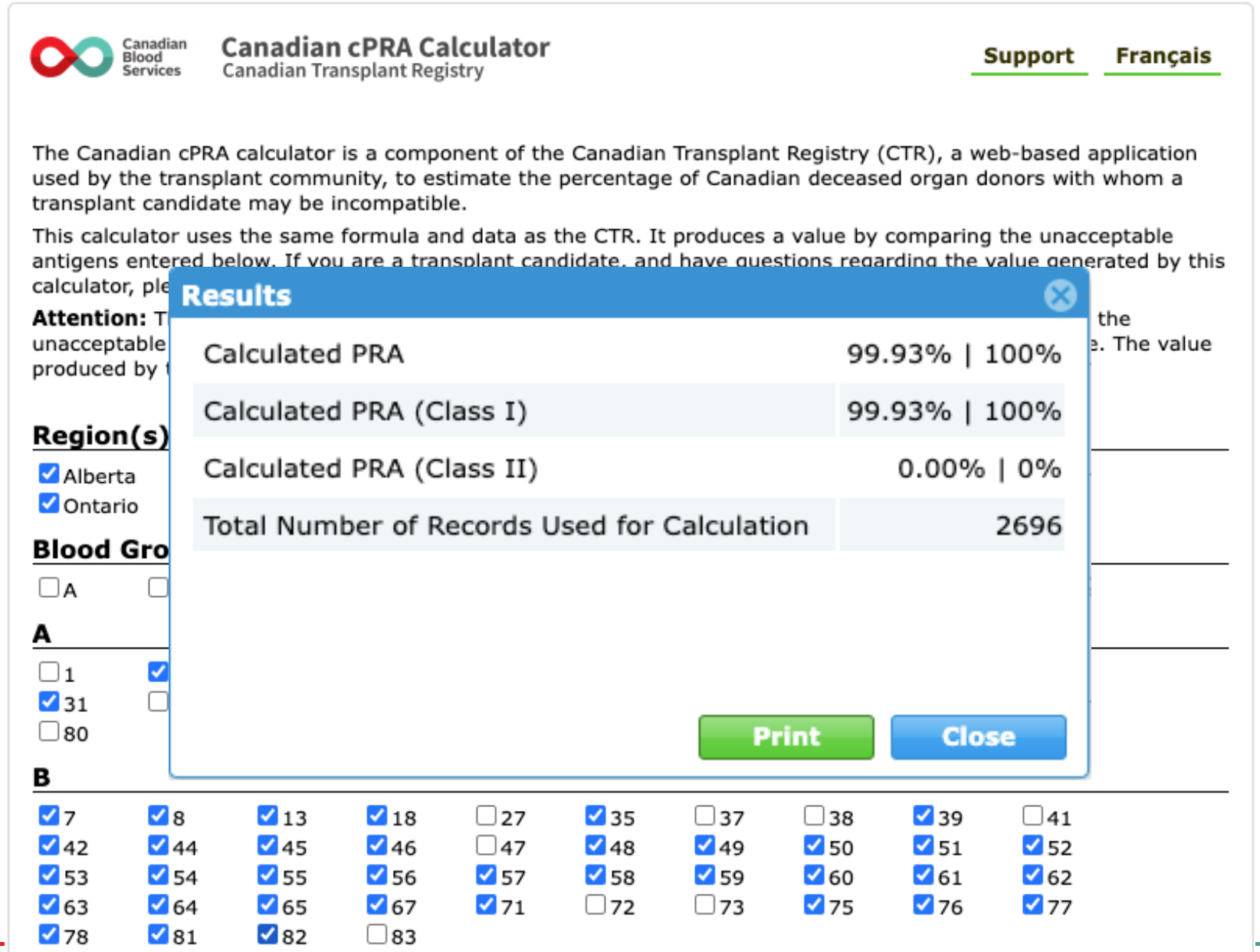
**Anti-HLA-A**: 2, 3, 11, 22, 25, 26, 29, 30, 31, 33, 34, 43, 66, 68, 69

**Anti-HLA-B**: 13, 18, 35, 39, 42, 44, 45, 46, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 67, 7, 71, 75, 76, 77, 78, 8, 81, 82

## HLA Typing

A24, A32

B27, B37


Canadian Blood Services
Canadian cPRA Calculator
Canadian Transplant Registry
Support
Français
The Canadian cPRA calculator is a component of the Canadian Transplant Registry (CTR), a web-based application used by the transplant community, to estimate the percentage of Canadian deceased organ donors with whom a transplant candidate may be incompatible.
This calculator uses the same formula and data as the CTR. It produces a value by comparing the unacceptable antigens entered below. If you are a transplant candidate, and have questions regarding the value generated by this calculator, ple
Attention: T
unacceptable
produced by
the
e. The value
Region(s)
Alberta
Ontario
Blood Gro
A
A
1
31
80
B
7 8 13 18 27 35 37 38 39 41
42 44 45 46 47 48 49 50 51 52
53 54 55 56 57 58 59 60 61 62
63 64 65 67 71 72 73 75 76 77
78 81 82 83
Results
Calculated PRA 99.93% | 100%
Calculated PRA (Class I) 99.93% | 100%
Calculated PRA (Class II) 0.00% | 0%
Total Number of Records Used for Calculation 2696
Print
Close

# PLATELET DONOR SELECTION (PDS)



Canadian Blood Services

Platelet Donor Selection
Match Donor Report
CBS Confidential Data

Version 4.0.0
2023-11-22 14:48

## Patient Info

| | | | |
|---|---|---|---|
| Patient ID: | [redacted] | A: | 1, - |
| Patient Name: | | B: | 8, 58 |
| Date of Birth: | | | |
| Blood Group: | | | |
| HPA: | | | |
| Report Notes: | PDS List based on antibody report from PI Lab sample dated 2023-11-14. All antibodies have been excluded. Only donors known to be HPA-1a/1a are included. pb 2023-11-22 | | |

## Match Options

| | | | |
|---|---|---|---|
| Centre(s): | All | | |
| Blood Group(s): | All | | |
| Match Type(s): | All | | |
| A Exclusion(s): | 2, 203, 210, 3, 9, 10, 11, 19, 23, 24, 2403, 25, 26, 28, 29, 30, 31, 32, 33, 34, 36, 66, 6601, 6602, 68, 69, 74, 80 | | |
| B Exclusion(s): | 5, 7, 703, 12, 13, 15, 17, 21, 22, 27, 2708, 35, 40, 4005, 41, 44, 45, 46, 47, 48, 49, 50, 51, 5102, 5103, 53, 56, 57, 60, 61, 62, 63, 67, 70, 71, 72, 73, 75, 76, 77, 78, 81, 82 | | |
| CREG Exclusion(s): | None | | |
| HPA Inclusion(s): | 1a/1a | Exclude Females: | No |
| Exclude RH+: | No | Exclude CMV+: | No |
| Max Donors: | 100 | Order By: | Quality, Centre |

## Results Summary

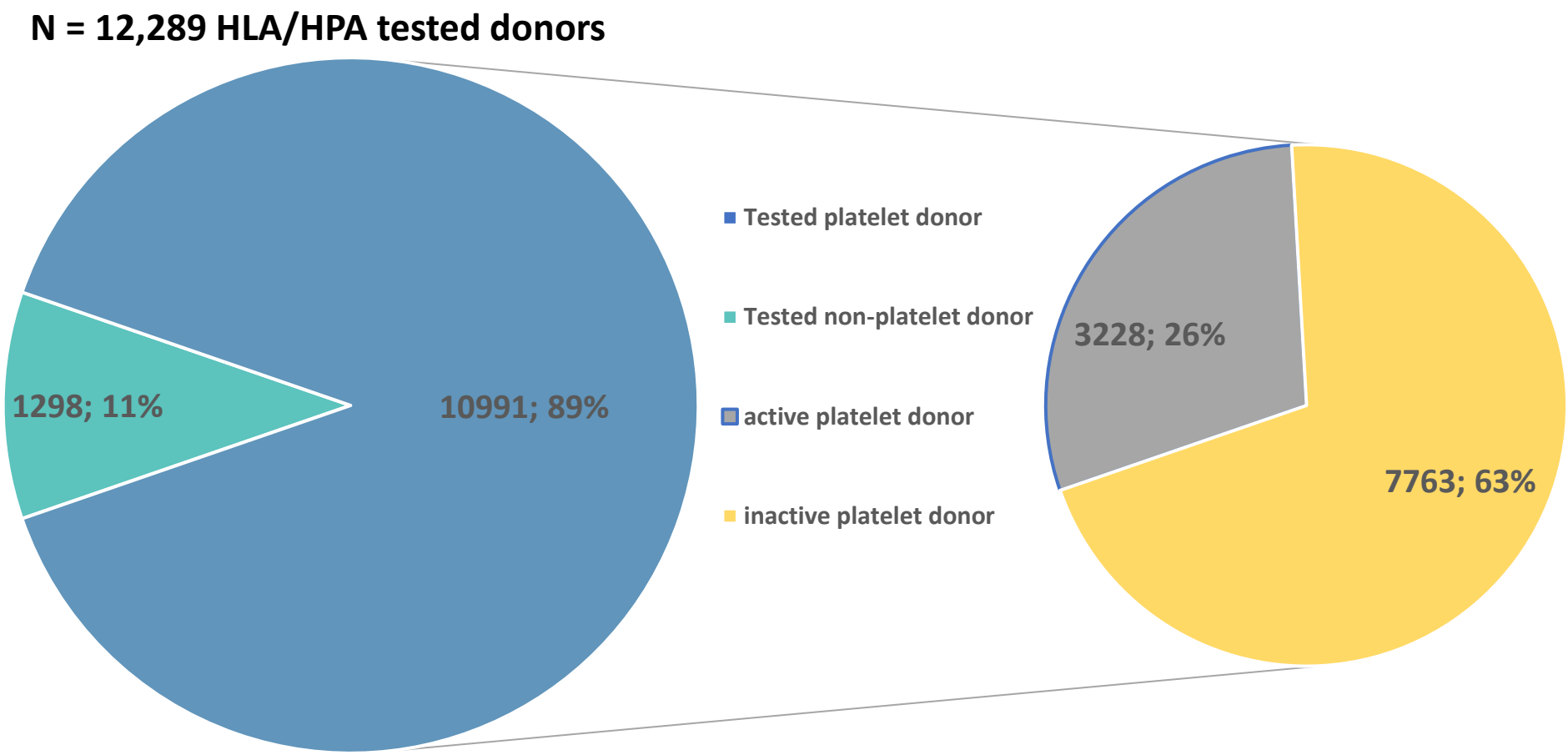
| Match Group | Registry Total | Report Total | Match Group | Registry Total | Report Total |
|---|---|---|---|---|---|
| MMMM | 45 | 45 | AAAN | 0 | 0 |
| MMMA | 15 | 15 | MMNN | 0 | 0 |
| MMAA | 1 | 1 | MANN | 0 | 0 |
| MAAA | 0 | 0 | AANN | 0 | 0 |
| AAAA | 0 | 0 | MNNN | 0 | 0 |
| MMMN | 0 | 0 | ANNN | 0 | 0 |
| MMAN | 0 | 0 | NNNN | 0 | 0 |
| MAAN | 0 | 0 | | | |
| | | | Registry Total: | | 61 |
| | | | Report Total: | | 61 |

## Legend

| Match Group | Match Type | Don. Type (Donation Type) | |
|---|---|---|---|
| (M) = Matched | (I) = Identical Match | (*) = Not drawn | (F) = Directed/Apheresis platelet |
| (A) = Acceptable | (P) = Possible Match | (A) = Autologous | (M) = Malaria (accepted donor) |
| (N) = Non-match | (B) = Broad Group Match | (C) = Concurrent plasma | (P) = Apheresis plasma |
| | (C) = Creg group Match | (D) = Directed/whole blood | (R) = Dry pack |
| | (N) = Non-match | (E) = Apheresis platelet | (S) = Specimen only |
| | | | (W) = Whole blood |

| Match Type | Donor Id / Centre | F. Name / L. Name | Gen. | H. Phone / B. Phone | Don. Date / Don. Type | ABO/Rh / CMV | A | B | Bw | Cw | DR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| IIII | [redacted] | | M | [redacted] | 2023-06-26 | A+ | 1 | 8 | - | - | - |
| | CAL | [redacted] | | | W | - | - | 58 | - | - | - |
| HPA(s): 1a/1a(d) | | | | | | | | | | | |
| IIII | [redacted] | | F | [redacted] | 2019-11-28 | O+ | 1 | 8 | 6 | - | - |
| | CAL | [redacted] | | | W | - | - | - | - | - | - |
| HPA(s): 1a/1a(d) | | | | | | | | | | | |
| IIII | [redacted] | | M | [redacted] | 2023-11-06 | O+ | 1 | 8 | - | - | - |
| | CAL | [redacted] | | | E | + | - | - | - | - | - |
| HPA(s): 1a/1a(d) | | | | | | | | | | | |
| IIII | [redacted] | | M | [redacted] | 2023-11-13 | B+ | 1 | 8 | - | - | - |
| | EDM | [redacted] | | | E | + | - | - | - | - | - |
| HPA(s): 1a/1a(d) | | | | | | | | | | | |
| IIII | [redacted] | | M | [redacted] | 2022-09-08 | A- | 1 | 8 | - | - | - |
| | EDM | [redacted] | | | E | - | - | - | - | - | - |
| HPA(s): 1a/1a(d) | | | | | | | | | | | |

# HLA Platelet Donors tested for HLA/HPA at CBS

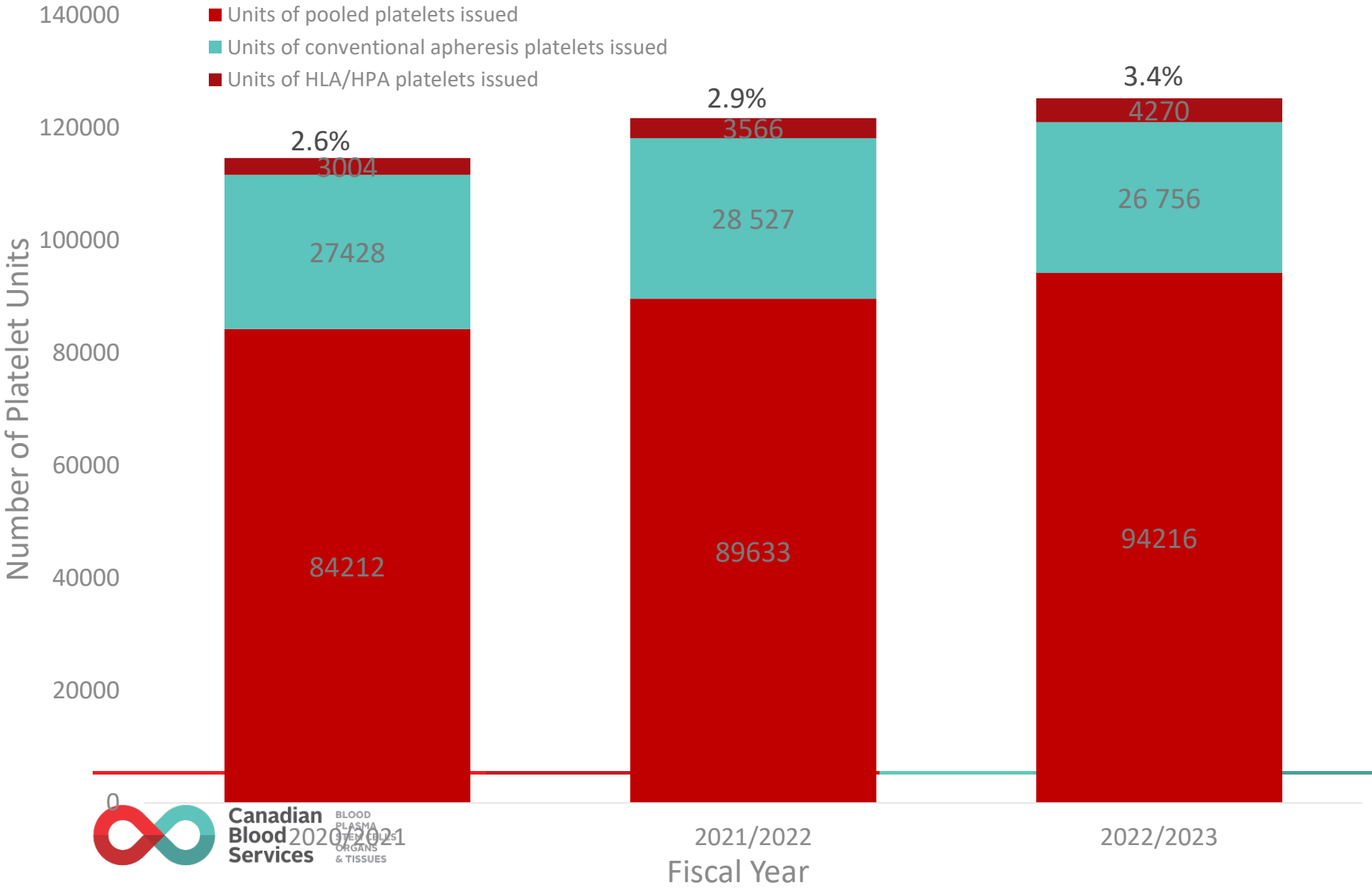



Canadian Blood Services
BLOOD PLASMA STEM CELLS ORGANS & TISSUES

# HLA ‘matching’ vs antigen avoidance

- **Matching**
  - Requires HLA typing
  - Narrows pool eligible donors
  - Higher chance of response
- **Avoidance**
  - Only need HLA Ab ID
  - Less restrictive than matching
  - Possibility of sensitization

# Number of HLA/HPA-matched Platelet Issued




- Approximately 3% of all platelets released by CBS are HLA/HPA-selected platelets.
- Proportions are increased gradually.

# Future strategies in HLA alloimmunization

**Mitigation**

Widen PLT donor pool

IgG removal/interference: eg IVIG/PLEX

B cell suppression (antiCD20, CD38)

Anticomplement Rx eg Eculizumab

IgG cleavage (IdeS)

**Prevention**

Class I HLA antigen depletion (citric acid)

Universal PLTs from IPSCs

Canadian Blood Services BLOOD PLASMA STEM CELLS ORGANS & TISSUES

Couvidou A et al. Front Immunology 2023
Jang D, Panch S. ASH ED 2022

# Objectives for today

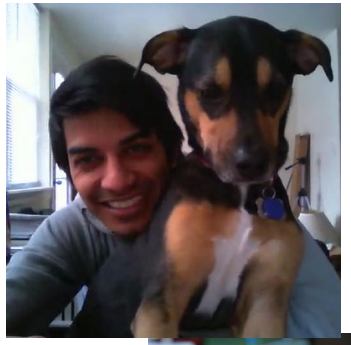
1. Review trends in platelet transfusion practice

2. Review causes and patterns of platelet transfusion refractoriness

3. Outline diagnosis and management of PLT refractoriness caused by alloimmunization

# Acknowledgements

Dr Akash Gupta



Plt Immunology Lab director, CBS

Natasha Rickards, RN

Transfusion Medicine Nurse Specialist Supervisor, CBS

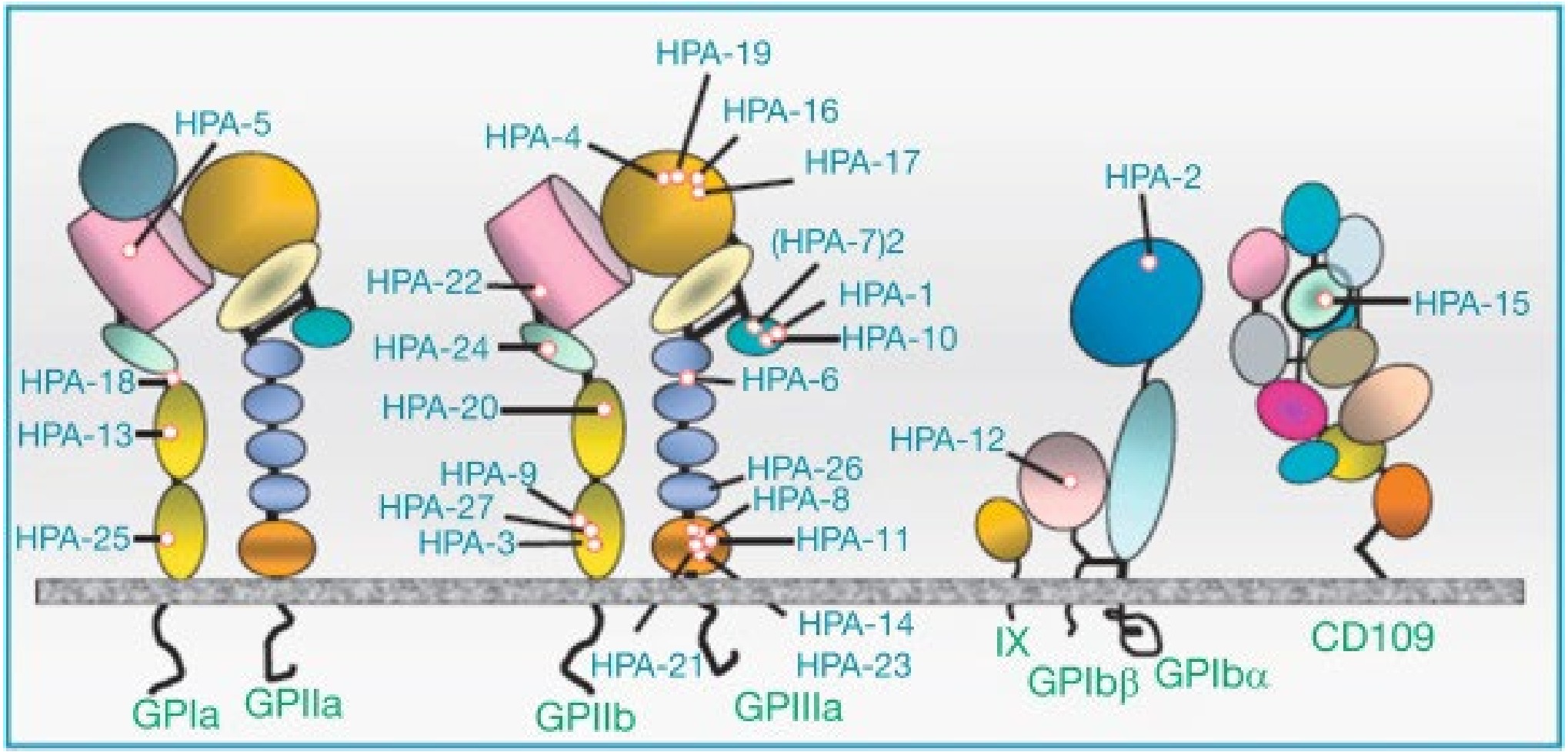
Dr Nancy Hua

Haempath resident, Univ of Alberta

# Questions?

# Extra slides

# What next?






M.-H. Tran, in Pathobiology of Human Disease, 2014

# HPA Testing

# HPA testing: similar to HLA

## Antibody screening

- PAKLx (flow cytometry), PAK Plus (ELISA)
- Monoclonal Antibody Immobilization of Platelet Antigens

## HPA typing

- Molecular assays that detect 22 HPA (1-9, 11, and 15)
- Identifies presence or absence of the polymorphisms using PCR

# Platelet Allo-Immunization

## NATIONAL PLATELET IMMUNOLOGY REFERENCE LABORATORY REPORT

Platelet Alloimmunization Investigation Report

### HPA Genotyping

| Name / ID / Relationship | Test / Sample Date | HPA-1 | HPA-2 | HPA-3 | HPA-4 | HPA-5 | HPA-6 | HPA-7 | HPA-8 | HPA-9 | HPA-11 | HPA-15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | HPA Beadchip | AA | AA | BB | AA | AA | AA | AA | AA | AA | AA | AB |
| Patient | 2023/11/14 | | | | | | | | | | | |

*All HPA Genotyping performed by Beadchip Microarray and/or PCR-SSP.*

### HPA Antibody

| Test | Sample Date | Sample Number | Result | Comments |
|---|---|---|---|---|
| PAKLx | 2023/11/14 | 23-00940 | 1b | |

*HPA Antibody testing performed by Luminex and/or ELISA.*

### Molecular HLA Typing

| Name / ID / Relationship | Sample Date | A* | B* | C* | DRB1* | DRB3* | DRB4* | DRB5* | DQA1* | DQB1* |
|---|---|---|---|---|---|---|---|---|---|---|
| Patient | 2023/11/14 | 01(1) | 08(8)<br>58(58) | | | | | | | |

*Local HLA Typing performed by PCR-SSO and/or PCR-SSP. HLA Typing results are displayed as molecular with serological equivalents in parentheses.*

# Case 2

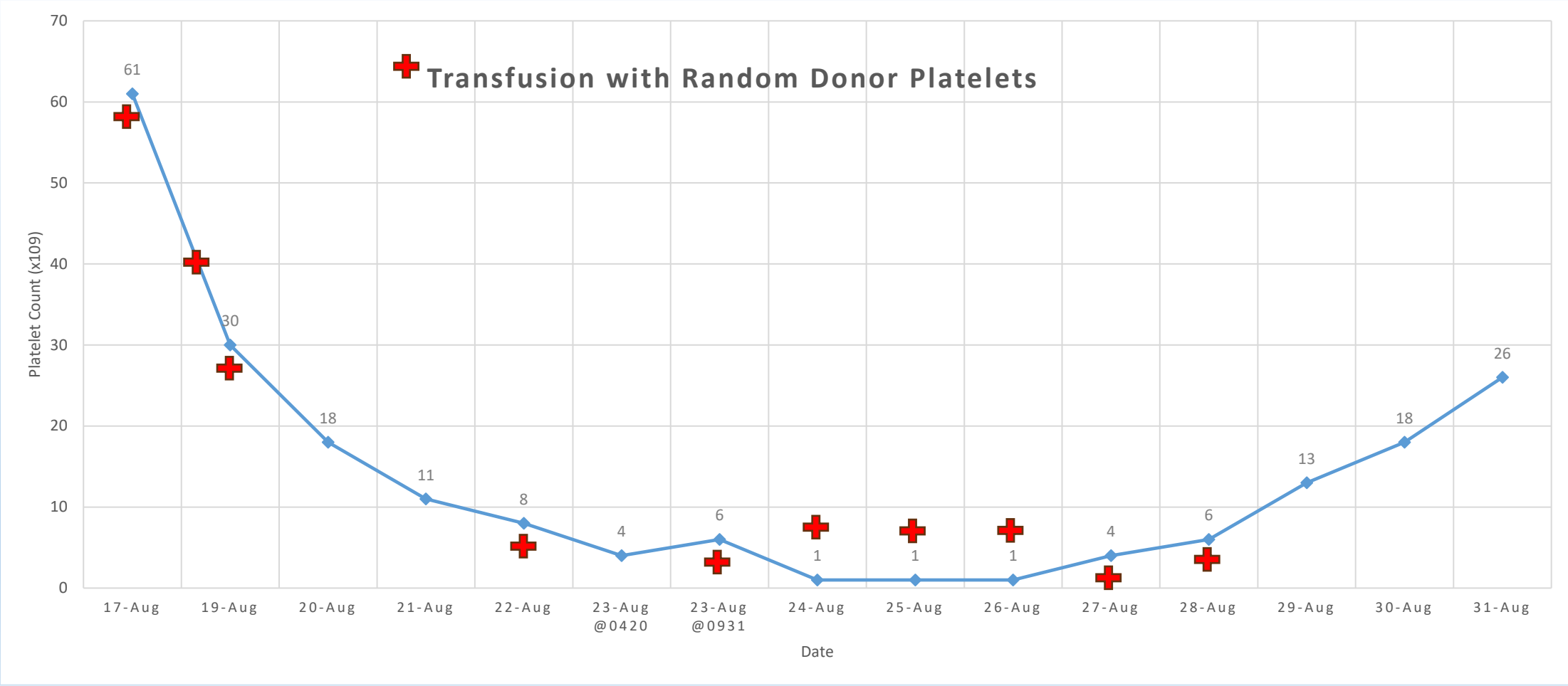
- HPA testing identified anti-HPA-1b antibody
- In addition to HLA antigens, only HPA-1a/1a platelets selected

- **Better increments observed**

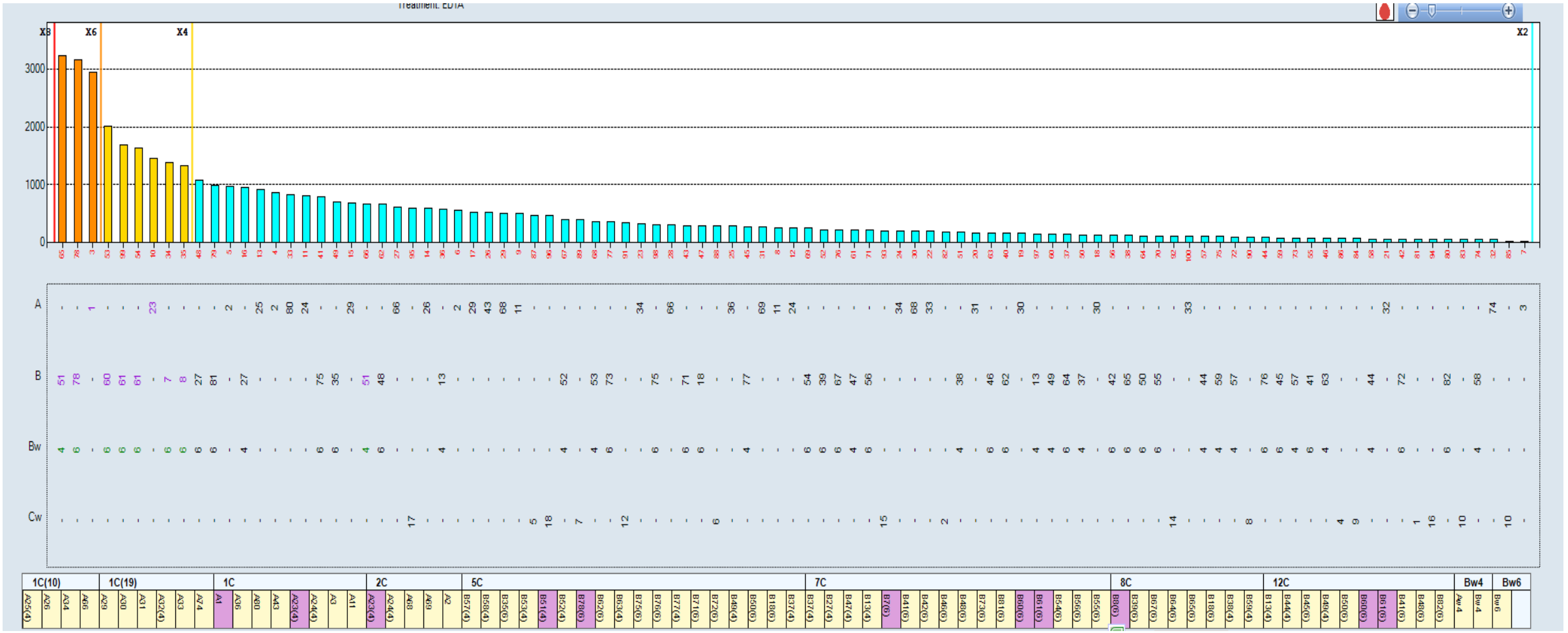
# Case 3

- 5-year-old female
- African (Cameroon) descent
- Diagnosis – AML
- Completed 2 cycles of chemotherapy, awaiting count recovery

# RANDOM PLATELET TRANSFUSIONS



# PLATELET ALLOIMMUNIZATION INVESTIGATION – TESTING - HLA Antibody Analysis – Fusion (One Lambda)



# PLATELET ALLOIMMUNIZATION INVESTIGATION – TESTING – HPA Antibody Analysis – MATCHIT! (werfen)

PAK Lx SAMPLE ANALYSIS AND RESULTS | Batch Name: Pak Lx Run #1 2023-08-25 | Assay Date: 08-25-2023

PAK Lx Kit Lot #: 3013670-PLX | Assay Tech: | Analysis Date: 2024/05/01

SAMPLE ID: 23-00379
Patient Name: 23-00379

Minimum Cutoff (MC). If the MFI of the Con beads is < MC, the Adjusted Ratios are calculated using MC. 188

| Antibody Target | GPIV | HLA | GPIIbIIIa (HPA-1,-3,-4) | GPIbIX (HPA-2) | GPIaIIa (HPA-5) |
|---|---|---|---|---|---|
| Result | Pos | Neg | Neg | Neg | Neg |

| Bead Region | Glycoprotein Group | Antigen | MFI | Bead Reactivity | Adjusted Ratio 1 | Adjusted Ratio 2 | Adjusted Ratio 3 |
|---|---|---|---|---|---|---|---|
| 13 | Con1 | Con1 | 143 | | | | |
| 14 | Con2 | Con2 | 133 | | | | |
| 18 | Con3 | Con3 | 114 | | | | |
| 11 | POS | POS | 12355 | | | | |
| 6 | GPIV | GPIV | 4028 | Positive | 18.87 | 18.87 | 18.82 |
| 10 | HLA Class I | HLA Class I | 151 | Negative | -1.75 | -1.74 | -1.7 |
| 21 | GPIIb-IIIa | HPA - 1a-3a-4a | 269 | Negative | -1.31 | -1.5 | -1.35 |
| 22 | GPIIb-IIIa | HPA - 1a-3b-4a | 268 | Negative | -1.43 | -1.59 | -1.48 |
| 23 | GPIIb-IIIa | HPA - 1b-3a-4a | 214 | Negative | -1.47 | -1.51 | -1.5 |
| 24 | GPIIb-IIIa | HPA - 1b-3b-4a | 208 | Negative | -1.54 | -1.62 | -1.77 |
| 25 | GPIIb-IIIa | HPA - 1ab-3ab-4a | 269 | Negative | -1.13 | -1.32 | -1.25 |
| 26 | GPIIb-IIIa | HPA - 1a-3ab-4b | 272 | Negative | -1.43 | -1.56 | -1.4 |
| 27 | GPIb/IX | HPA - 2a | 136 | Negative | -1.38 | -1.4 | -1.34 |
| 28 | GPIb/IX | HPA - 2a | 136 | Negative | -1.22 | -1.25 | -1.2 |
| 29 | GPIb/IX | HPA - 2ab | 115 | Negative | -1.52 | -1.63 | -1.53 |
| 30 | GPIb/IX | HPA - 2b | 124 | Negative | -1.36 | -1.43 | -1.32 |
| 32 | GPIb/IX | HPA - 2b | 142 | Negative | -1.08 | -1.13 | -1.12 |
| 33 | GPIa-IIa | HPA - 5a | 266 | Negative | -1.38 | -1.34 | -1.36 |
| 42 | GPIa-IIa | HPA - 5a | 239 | Negative | -1.23 | -1.25 | -1.3 |
| 48 | GPIa-IIa | HPA - 5ab | 251 | Negative | -1.49 | -1.56 | -1.4 |
| 51 | GPIa-IIa | HPA - 5b | 232 | Negative | -1.54 | -1.46 | -1.69 |
| 54 | GPIa-IIa | HPA - 5b | 315 | Negative | -1.08 | -1.22 | -1.11 |

# PLATELET ALLOIMMUNIZATION INVESTIGATION INTERIM REPORT

## NATIONAL PLATELET IMMUNOLOGY REFERENCE LABORATORY REPORT

Platelet Alloimmunization Investigation Report - INTERIM

### HPA Antibody

| Test | Sample Date | Sample Number | Result | Comments |
|---|---|---|---|---|
| PAKLx | 2023/08/23 | 23-00379 | GPIV | |

*HPA Antibody testing performed by Luminex and/or ELISA.*

### Molecular HLA Typing

| Name / ID / Relationship | Sample Date | A* | B* | C* | DRB1* | DRB3* | DRB4* | DRB5* | DQA1* | DQB1* |
|---|---|---|---|---|---|---|---|---|---|---|
| Patient | 2023/08/23 | 03(3)<br>74(74) | 45(45)<br>58(58) | | | | | | | |

*Local HLA Typing performed by PCR-SSO and/or PCR-SSP. HLA Typing results are displayed as molecular with serological equivalents in parentheses.*

### HLA Antibody

| Test | Sample Date | Sample Number | Result | Strong | Moderate | Weak | Comments |
|---|---|---|---|---|---|---|---|
| LSA- Class I | 2023/08/23 | 23-00379 | CPRA:<br>68 | | A:1<br>B:51 78 | A:23<br>B:60 61 7 8 | |

*All HLA antibody testing performed by Luminex.*
*Calculated PRA (cPRA) values are determined based on the Canadian Calculator using unacceptable, moderate, and weak antibody specificities.*

### Case Comments

Anti-GPIV (anti-CD36) detected. Referral testing to be forwarded to Versiti Wisconsin for confirmation.

HLA Class I antibodies detected.

### Other Comments

(MLT) notified of critical result on 2023-08-25 at 1630 (RBV).

# CD36 (GPIV)

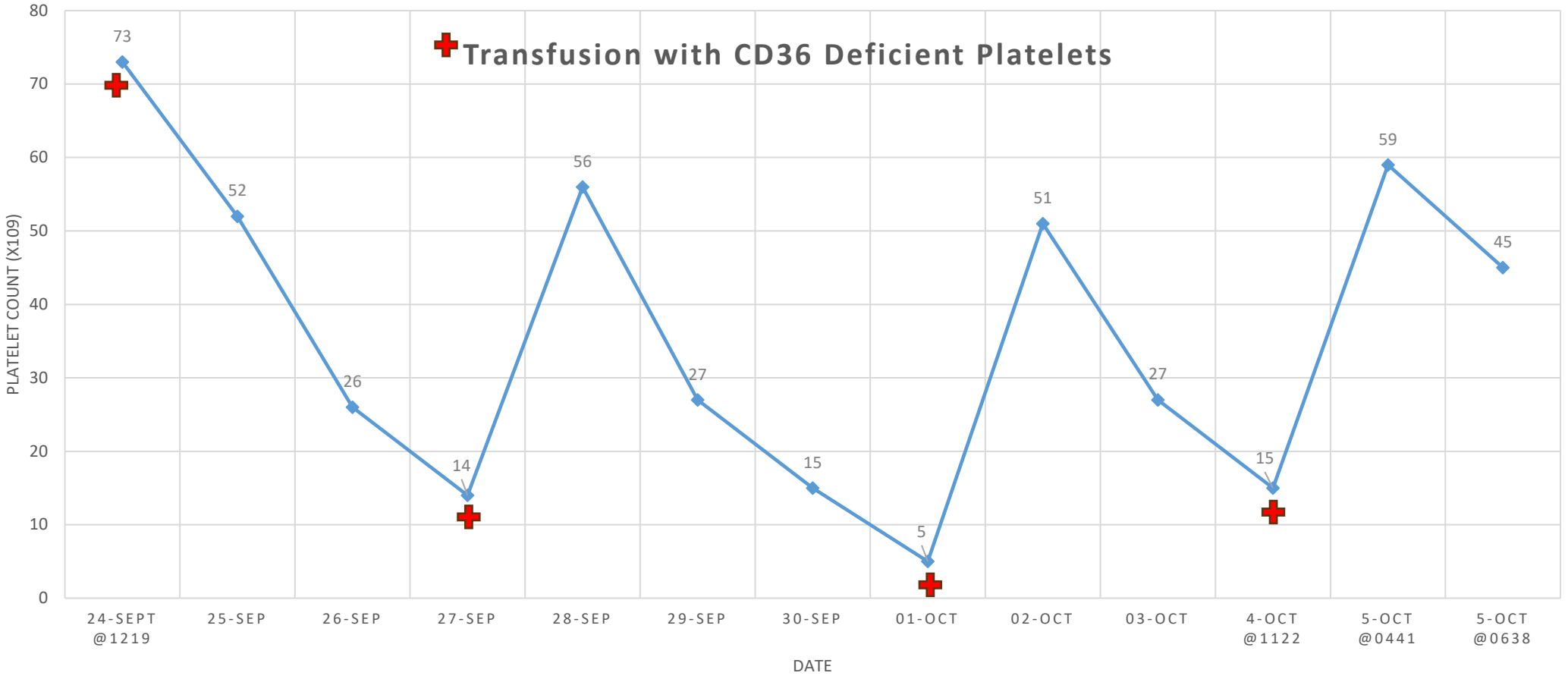
- Membrane protein expressed on phagocytes, platelets, RBC and some epithelia[1]
- Functions as receptor for certain adhesive proteins (microvascular endothelial cells)[2]
- Functions a transporter of long chain fatty acids (phagocytes)[2]
- Impacts immune system
- Deficiency more frequently found in  people of Black and Asian ancestry, rare in Caucasians

[1]Silverstein, Roy et al. Sci Signal 2009 May 26: 2(72):re3
[2]Chen, Yiliang et al. JEM 2022 Jun 6; 219(6): e20211214

# CD36 (GPIV) DEFICIENT PLATELETS

- Needed for cycle 3 chemotherapy
- None available in Canada – donors not tested for CD36
- US Blood Supplier: one donor available – HLA-permissive match

# CD36 (GPIV) DEFICIENT PLATELETS TRANSFUSIONS



# CONCLUSION

This case highlights:

- The need for platelet refractoriness testing for patients undergoing continual platelet transfusions
- The important clinical impact and significance of anti-CD36
- Rare platelets (CD36 deficient) available despite challenging and complex process required to import such platelets

# Objectives for today

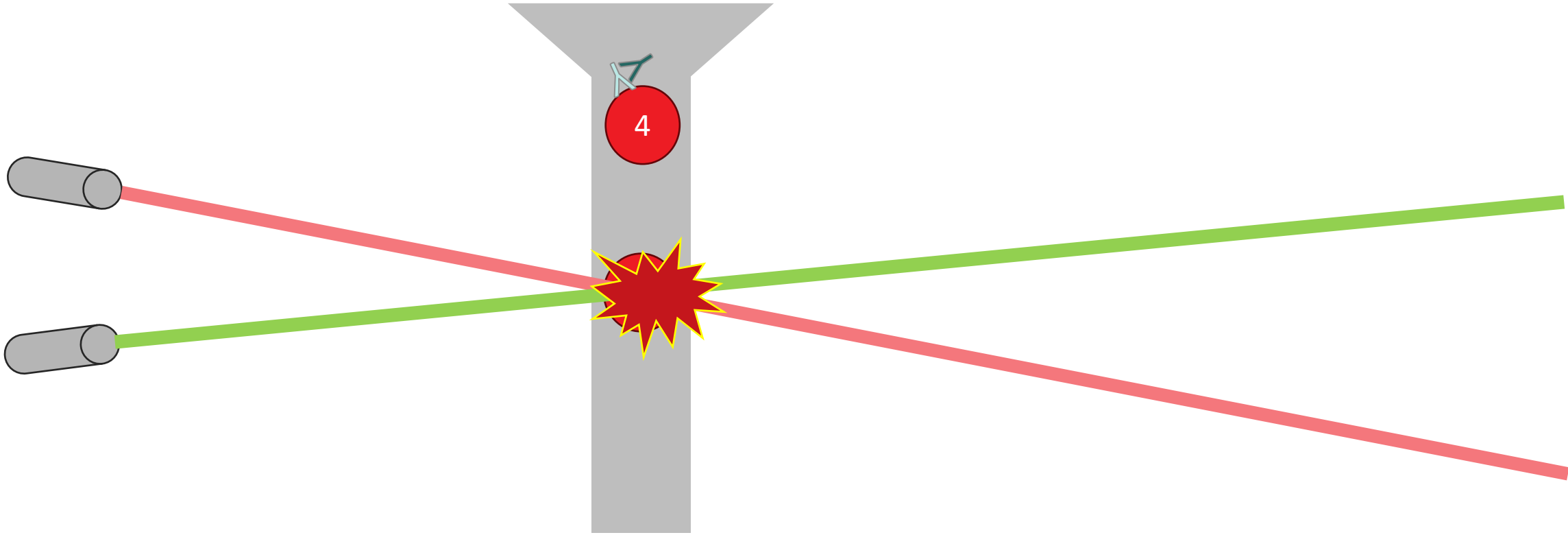
1. Review causes and patterns of platelet transfusion refractoriness – **immune vs non-immune**

2. Outline diagnosis and management of PLT refractoriness caused by alloimmunization – **HLA, HPA, donor selection**

3. Discuss challenging cases in the management of alloimmune refractoriness – **HLA +/- HPA, CD36 deficiency, future strategies**

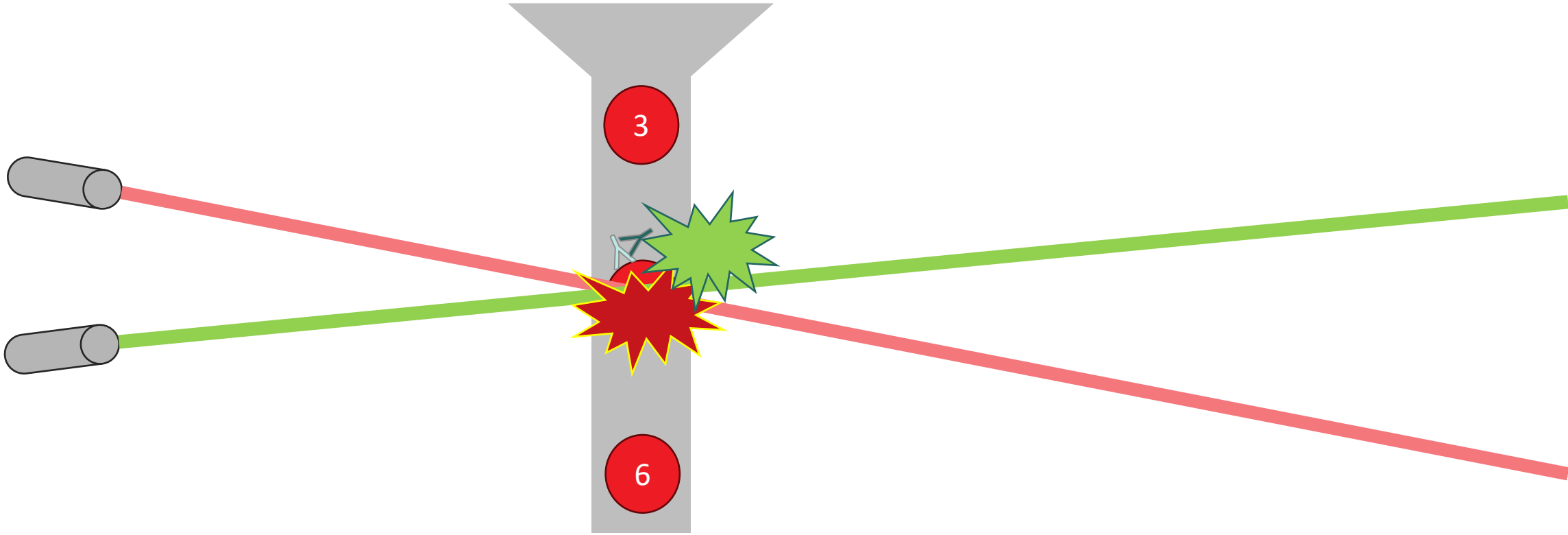
# Luminex: Red light, Green light

Two color flow cytometry used to identify each bead and determine if IgG present



# Luminex: Red light, Green light

Two color flow cytometry used to identify each bead and determine if IgG present



# A note about clinical efficacy - PLADO trial[13]

## Method

- Prophylactic platelet transfusion to hematologic cancer and solid tumor patients
- Received low ($1.1x10^{11}$), medium ($2.2x10^{11}$), or high ($4.4x10^{11}$) dose when platelet count was less than 10,000/L
- Primary endpoint: Grade 2 or higher bleeding defined by WHO

## Result

- Significant bleeding **did not** differ between groups

**Trials with pathogen-reduced platelets also did not observe an increased bleeding risk due to fewer platelets in a platelet dose.[8]**

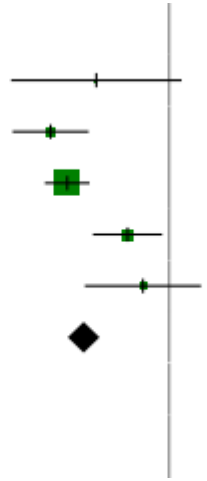
# INTERCEPT vs Untreated[6]

**1.21.2 Intercept plts vs standard plts - multiple platelet transfusion studies**

| | | | | | | |
|---|---|---|---|---|---|---|
| Janetzko 2005 | 22 | 11.6 (7.3) | 21 | 15.1 (6.4) | 3.47% | -3.5[-7.6,0.6] |
| Kerkhoffs 2010 | 85 | 11.4 (5.3) | 99 | 17.1 (7.3) | 17.46% | -5.7[-7.53,-3.87] |
| McCullough 2004 | 318 | 11.1 (6.1) | 327 | 16 (7.8) | 50.56% | -4.9[-5.97,-3.83] |
| Rebulla 2016 | 109 | 9.4 (5.3) | 107 | 11.4 (7) | 21.04% | -2[-3.66,-0.34] |
| van Rhenen 2003 | 52 | 12.5 (7.9) | 51 | 13.8 (6.5) | 7.47% | -1.26[-4.05,1.53] |
| **Subtotal ***** | **586** | | **605** | | **100%** | **-4.11[-4.87,-3.35]** |

Heterogeneity: $Tau^2=0$; $Chi^2=15.25$, df=4(P=0); $I^2=73.77\%$

Test for overall effect: Z=10.55(P<0.0001)



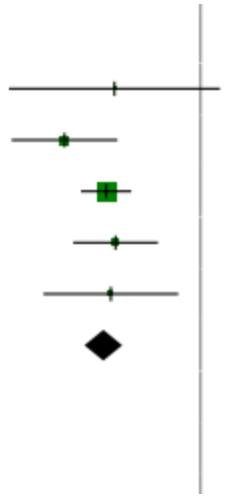
**1 hr CCI**

**1.23.2 Intercept plts vs standard plts - multiple platelet transfusion studies**

| | | | | | | |
|---|---|---|---|---|---|---|
| Janetzko 2005 | 22 | 7.3 (6.2) | 21 | 10.4 (6.5) | 2.06% | -3.1[-6.9,0.7] |
| Kerkhoffs 2010 | 85 | 7.9 (5.3) | 99 | 12.8 (7.8) | 8.2% | -4.9[-6.81,-2.99] |
| McCullough 2004 | 318 | 6.7 (5.6) | 327 | 10.1 (6.1) | 36.25% | -3.4[-4.31,-2.49] |
| Rebulla 2016 | 109 | 6.1 (4.5) | 107 | 9.2 (6.7) | 12.79% | -3.06[-4.59,-1.53] |
| van Rhenen 2003 | 52 | 7.3 (5.4) | 51 | 10.6 (7.1) | 5.05% | -3.23[-5.66,-0.8] |
| **Subtotal ***** | **586** | | **605** | | **64.36%** | **-3.5[-4.18,-2.82]** |

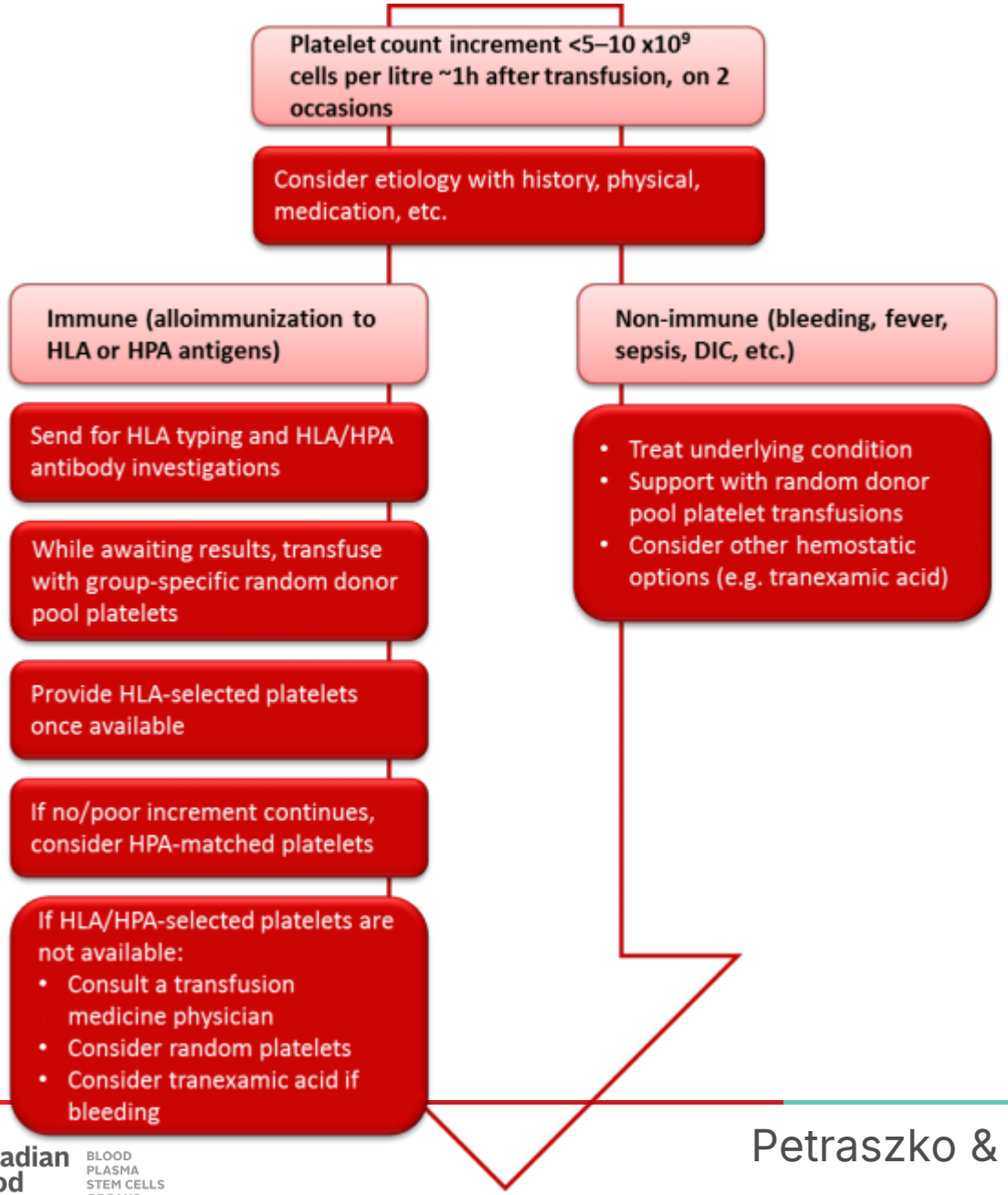
Heterogeneity: $Tau^2=0$; $Chi^2=2.53$, df=4(P=0.64); $I^2=0\%$

Test for overall effect: Z=10.09(P<0.0001)



**24 hr CCI**

Note: These studies are a mix of PAS and plasma PRT components; pooled and apheresis platelets




Petraszko & Zeller, 2018, CBS Prof Edu Chapter 18

# HLA/HPA Patient Diagnoses

2022/2023