SESSION COMMUNE SFTS/SFH TRANSFUSION ET APHÉRÈSE

Gestion des thrombopénies réfractaires et transfusion plaquettaire

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SESSION COMMUNE SFTS/SFH TRANSFUSION ET APHÉRÈSE

Gestion des thrombopénies réfractaires et transfusion plaquettaire

Qu'est-ce qu'un état réfractaire ?

Quelle prise en charge ?

Quelles alternatives ?

La place de l'hémaphérèse ?

Quelles perspectives ?

Qu’est-ce qu’un état réfractaire ?

Transfusion plaquettaire inefficace ?

Quelles caractéristiques du produit ?

1. Adapté au poids du patient
2. ABO compatible
3. Conservé moins de 72h

Quels outils de mesure de l’inefficacité ?

3 outils : PI, RTP, CCI

Qu’est-ce qu’un état réfractaire ?

Augmentation absolue de la numération plaquettaire

$$\mathrm{PI} = \text{posttransfusion platelet count} - \text{pretransfusion platelet count}$$

➡ **> 10** x 10^9 / L à **1h et 24h**

Rendement transfusionnel plaquettaire (RTP)

$$\mathrm{R}\ (\%) = \mathrm{PI} \times \mathrm{BV} \times \mathrm{PD}^{-1} \times 100$$

➡ **> 30% à 1h**, **>20% à 24h**

Corrected Count Increment (CCI)

$$CCI = \frac{(Absolute\ count\ increment,\ /\mu\mathrm{L}) \times (Body\ surface\ area,\ \mathrm{m}^2)}{(Number\ of\ platelets\ transfused,\ \times 10^{11})}$$

➡ **> 7,5** x 10^9 / L **à 1h** et **> 4,5** x 10^9 / L à **24h**

Stanworth, S. J., Br J Haematol (2015)
Panch, S. R., Blood Rev (2023)
Jaime-Pérez, Am J Clin Pathol (2018)

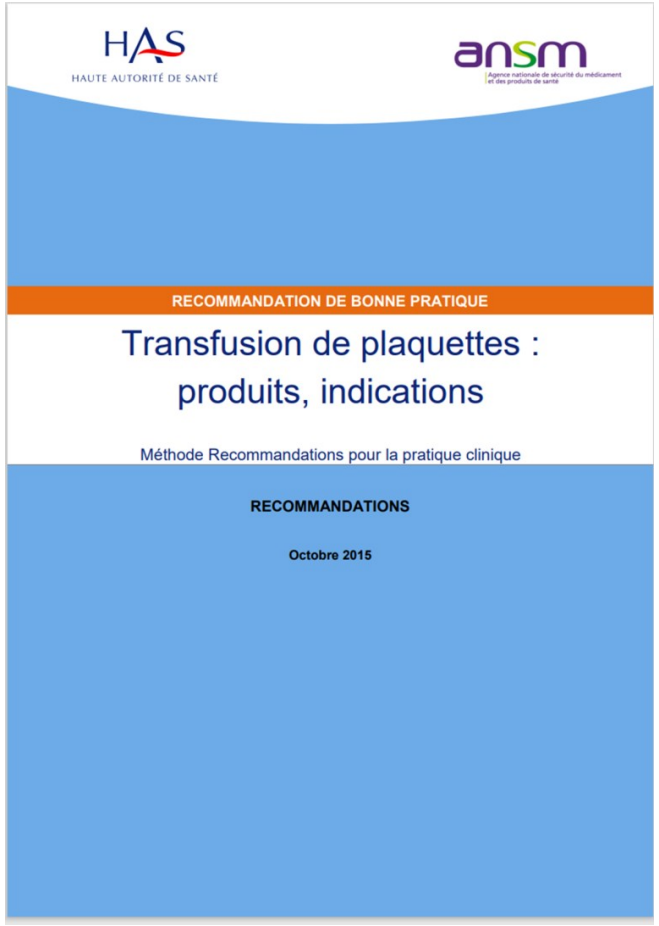
Variable	Formulae	Suggested cut-offs defining clinical refractoriness	
		1 h	16-24 h
Platelet Increment (PI)	Post-Pre	$<10 \times 10^9$/L	$<10 \times 10^9$/L
Percentage Platelet Recovery (PPR)	[PI × TBV* × 100%]/PD†	<20%	<10%
Corrected Count Increment (CCI)	[PI × BSA‡]/PD†	$<5 \times 10^9$/L/m^2	$<2.5 \times 10^9$/L/m^2

Belizaire, Transfusion Medicine Reviews (2020)

Qu’est-ce qu’un état réfractaire ?

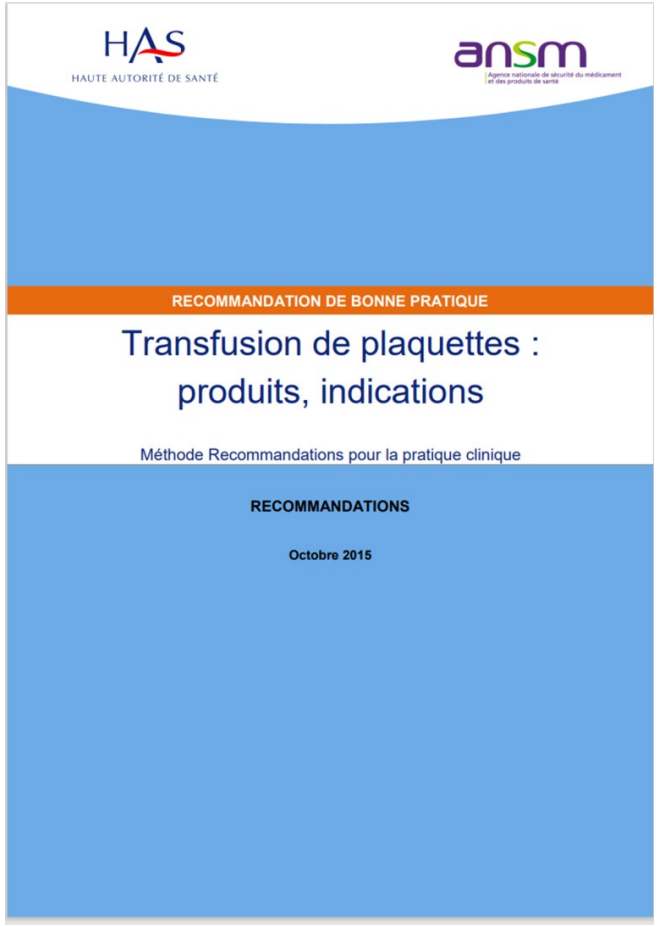
Etat réfractaire

Inefficacité transfusionnelle plaquettaire constatée après **deux** transfusions successives



AE	Une inefficacité transfusionnelle plaquettaire constatée après deux transfusions successives définit un état réfractaire. On parle d'inefficacité transfusionnelle plaquettaire quand après une 2e transfusion d'un nombre de CP adapté au poids du patient, ABO compatibles, et conservés depuis moins de 72 heures, le CCI est inférieur à 7.
AE	En cas d’augmentation inférieure à la valeur attendue, il est possible de calculer de façon précise le rendement plaquettaire par le calcul du *Corrected Count Increment* (CCI). $CCI = \frac{[NP \text{ après transfusion} - NP \text{ avant transfusion}] \times \text{surface corporelle } (m^2) \times 100}{\text{Nombre de plaquettes transfusées } (\times 10^{11})^*}$ Valeur attendue du CCI > 7 * Ce nombre figure sur les étiquettes des CPA et des MCP. NP exprimée en $G.L^{-1}$.

Qu’est-ce qu’un état réfractaire ?



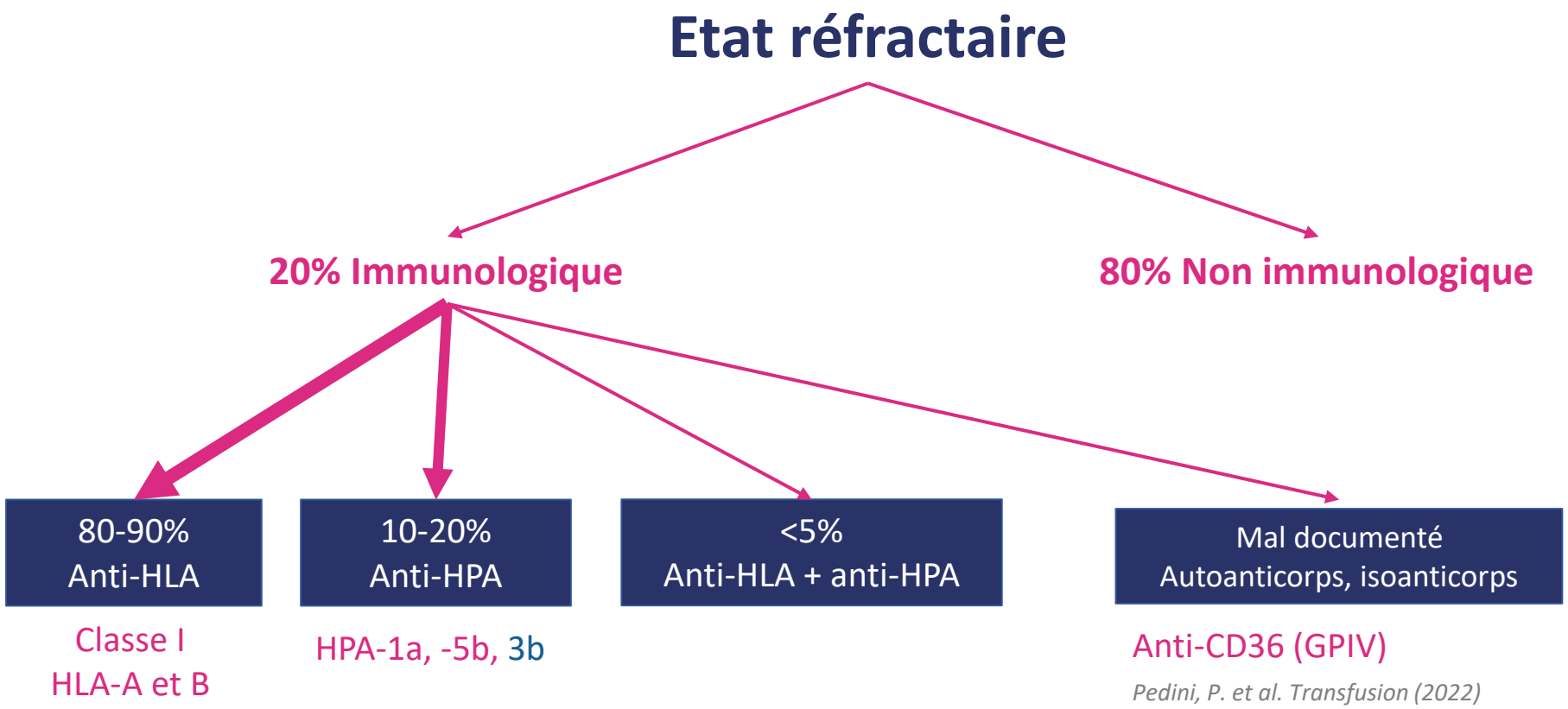
Etat réfractaire

80% Non immunologique

La cause immunologique d’un état réfractaire ne peut être retenue qu’après élimination d’une autre cause :

- fièvre, avec ou sans infection documentée ;
- coagulation intravasculaire disséminée ;
- splénomégalie ;
- complications d'une greffe de cellules souches hématopoïétiques (maladie veino-occlusive, infection à CMV, réaction du greffon contre l'hôte, micro-angiopathie thrombotique) ;
- interférence médicamenteuse ;
- qualité du produit transfusé : dose, compatibilité ABO et durée de conservation.

Qu’est-ce qu’un état réfractaire ?



Stanworth SJ, et al. *Br J Haematol* (2015)

Qu'est-ce qu'un état réfractaire ?

Etat réfractaire

20% Immunologique

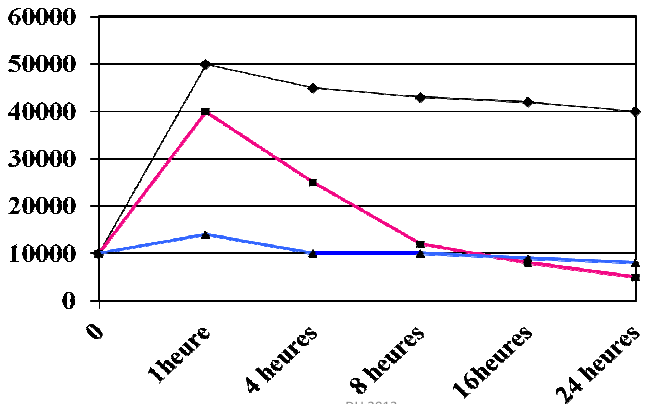
80% Non immunologique

Quand mesurer le CCI après la TP ?

24h : définition d'une inefficacité selon HAS

1h : Oriente vers une étiologie **immunologique**

10min ? 30min ? Mêmes performances qu'à 1h



Mesure de l'efficacité et de la recirculation

- NFS à **1 heure** : apprécie la **recirculation**
- NFS à **24 heures** : apprécie **l'efficacité**

Stanworth SJ, et al. *Br J Haematol* (2015), Matsui R, et al. *Transfusion and Apheresis Science* (2021

Qu’est-ce qu’un état réfractaire ?

Etat réfractaire

20% Immunologique

HLA, HPA, CD36

→ CCI bas dès 1h

80% Non immunologique

Consommation, destruction, séquestration

→ CCI ok à 1h
CCI bas à 24h

Slichter, S. J. et al. Blood (2005)
Daly, JAMA (1980)

Causes mixtes

Cohn, C. S et al.. Hematology (2020)

Barbagallo et al. Hematol Transfus Cell Ther (2022)

CCI non utilisable si saignements

Couvidou et al., Front. Immunol. (2023)

Quelle prise en charge ?

Pourquoi prendre en charge un ER ?

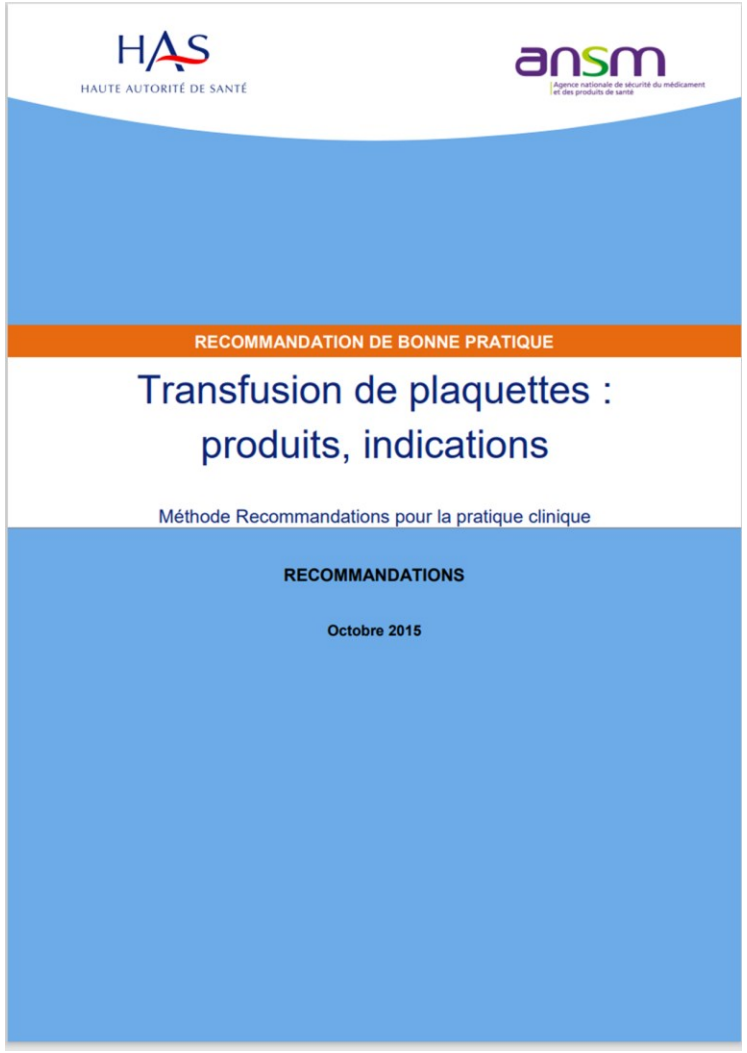
Conséquences médicales :

- Durée hospitalisation + longue en soins intensifs — *Song, X et al. 2023*
- Un risque accru de saignement — *Kerkhoffs et al, 2008*
- Coûts d'hospitalisation plus élevés — *Arabi, S. et al. 2021*
- Une diminution de la survie

Conséquences transfusionnelles :

- ER associé à plus de transfusions — *Meehan et al, 2000*

Quelle prise en charge ?



Comment prendre en charge un ER ?

Deux situations imposent le recours au CPA :	
A	Chez les patients porteurs d'anticorps anti-HLA et/ou HPA responsables d'un état réfractaire, il est recommandé de rechercher des donneurs de phénotype HLA et/ou HPA identiques ou proches de celui du patient, afin de transfuser des CPA les plus compatibles possible. Ces donneurs sont prélevés par aphérèse pour préparer un CPA.

Indication des CPA HLA compatible :

Anticorps anti-HLA + État réfractaire

Quelle prise en charge ?

TABLE 3. Response to PLT transfusion

	RAPs	HLA-selected PLTs	PPs
Number of PLT units transfused	77	412	388
CCI per PLT unit			
Mean (±SD)*	2.82 (±5.82)	11.44 (±8.12)	4.77 (±6.93)
Median (range)	0.89 (−9.72 to 20.34)	10.09 (−5.51 to 47.53)	2.60 (−16.66 to 46.55)
Number of patients receiving each type of PLT †	41	60	81
CCI per patient, mean (±SD)	2.82 (±5.93)	13.92 (±7.64)	4.46 (±5.16)
Successful transfusions‡	24 (31%)	330 (80%)	136 (35%)

* $p < 0.0001$ when comparing all three mean CCIs. This difference remained significant when comparing RAPs versus HLA-selected PLTs ($p < 0.001$) and PPs versus HLA-selected PLTs ($p < 0.001$) but not when comparing RAPs versus PPs ($p > 0.05$).

† $p < 0.0001$ when comparing all three mean CCIs per patient. This difference remained significant when comparing RAPs versus HLA-selected PLTs ($p < 0.001$) and PPs versus HLA-selected PLTs ($p < 0.001$) but not when comparing RAPs versus PPs ($p > 0.05$).

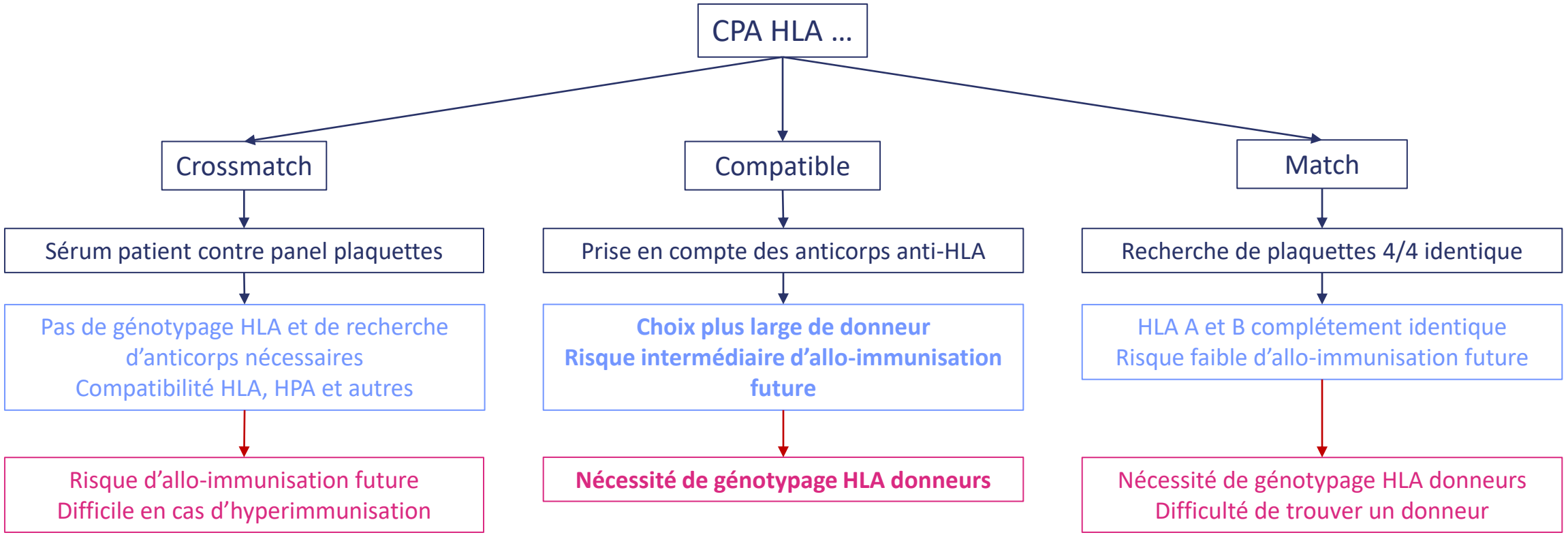
‡ $p < 0.0001$ when comparing success rate of all three types of PLTs. This association remained significant when comparing RAPs versus HLA-selected PLTs ($p < 0.0001$) and PPs versus HLA-selected PLTs ($p < 0.0001$) but not when comparing RAPs versus PPs ($p = 0.51$).

Meilleure efficacité des CPA HLA compatible chez patients immunisés

vs CPA non HLA et vs MCP

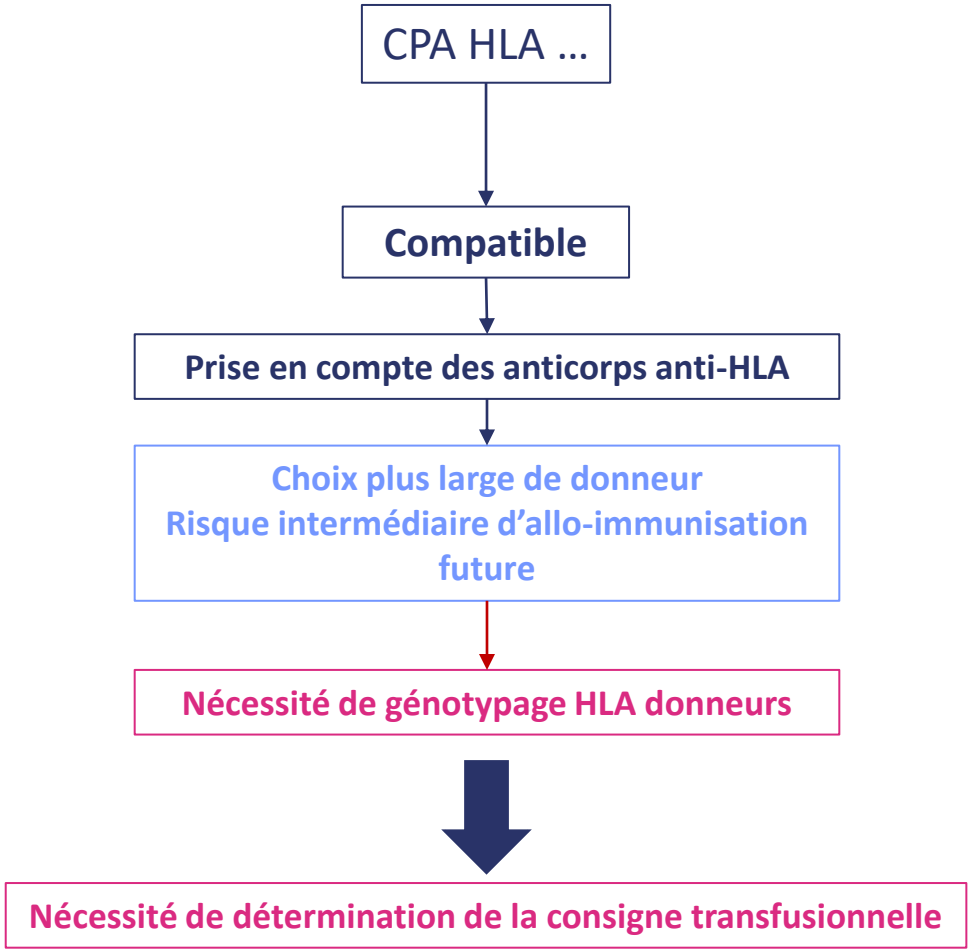
C. Gavva et al, Transfusion 2019

Quelle prise en charge ?



Basire, A. & Picard, C. Transfus Clin Biol (2014)
Seike, K. et al. Transfusion (2020)
Cohn, C. S. Hematology (2020)
Garraud, O. et al. (2023)

Quelle prise en charge ?



Quelle prise en charge ?

Table 3. Corrected count increments (CCI), absolute count increments (ACI) and the percentage of the transfusions reaching the given response threshold at 18–24 h after HLA-selected platelet transfusion

	CCI[1] median (range)	CCI >5·0 % of transfusions	ACI[2] 10^9/L median (range)	ACI > 15 × 10^9/L % of transfusions	No of platelets transfused ×10^{11}/m^2	Number of transfusions
HLA identical	13·0 (−16·6 to 45·2)	89%	36 (−61 to 103)	86%	2·6 (1·5 to 3·7)	50
HLA acceptable	12·8 (−3·8 to 40·4)	80%	34 (−11 to 123)	76%	2·7 (1·9 to 3·5)	45
HLA mismatch						
MFI 200–1000	10·3 (−4·1 to 27·5)	74%	25 (−11 to 92)	72%	2·6 (2·1 to 3·9)	35
MFI >1000	7·6 (−8·4 to 30·7)	56%	21 (−28 to 88)	54%	2·6 (1·6 to 3·7)	86
MFI >5000	1·5 (−7·4 to 12·2)	26%	4 (−15 to 34)	21%	2·5 (1·8 to 3·7)	20

Responses are shown according to the HLA matching of the donors.
[1]Good CCI response at 18–24 h post-transfusion 5·0 × 10^9/L or more.
[2]Good ACI response at 18–24 h post -transfusion 15 × 10^9/L or more.

Les anticorps anti-HLA impactent l'efficacité
Plus la MFI est élevée moins l'efficacité est bonne

T Linjama et al, British Blood Transfusion Society 2017

Quelle prise en charge ?

Consigne en fonction d'un compte rendu :

IDENTIFICATION des ANTICORPS ANTI-HLA CLASSE I: TECHNIQUE de HAUTE DEFINITION

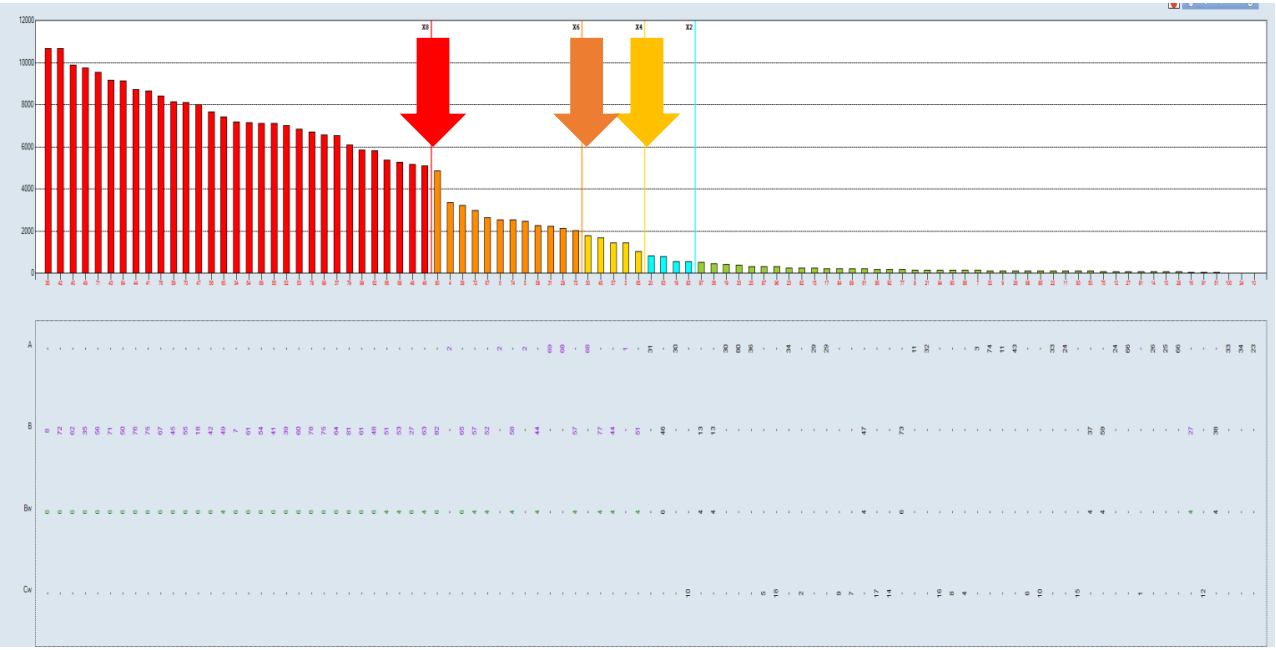
Technique LUMINEX "single antigen" ONE LAMBDA (prétraitement du sérum à l'EDTA)

Pourcentage de billes positives : 49 % du Panel

Spécificités des Anticorps IgG Anti - HLA Classe I identifiées : A1 A2 A68 A69 B7 B8 B18 B35 B39 B41 B42 B44 B45 B48 B49 B50 B51 B52 B53 B54 B55 B56 B57 B58 B60 B61 B62 B63 B64 B65 B67 B71 B72 B75 B76 B77 B78 B81 B82 "Bw6" B*27:08

→ 0 donneur en région
12 donneurs en France

Consigne dynamique DIST-HLA-Prélèvement :



→ **MFI 1 000 :**
0 donneur en région
12 donneurs en France

→ **MFI 2 000 :**
138 donneurs en région
> 1 000 donneurs en France

MFI 5 000 :
504 donneurs en région

+ prise en compte du typage du patient, CREG, épitopes …

Quelle prise en charge ?

Article de revue

Pavenski, K. et al. Transfusion (2013)

Transfusion HLA compatible :

- Augmente la CCI
- Diminue le nombre de transfusions

TABLE 4. PLT increments in nonrandomized studies

Author, year	PLT count increment
Prospective	
Marktel, 2010[24]	IR, LR, SDP HLA matched CCI > 4.5 in 74% Median increment: 43.5 × 10^9/L with HLA matched vs. CCI > 4.5 in 59% Median increment: 36.5 × 10^9/L for HLA 1 mismatch vs. CCI > 4.5 in 26% and Median increment: 6.25 × 10^9/L with RDP; p < 0.01 for HLA vs. RDP, p = 0.02 for random vs. HLA mismatch, p = 0.16 for HLA vs. HLA mismatch IR, LR non–HLA-matched RDP CCI > 4.5 in 74% Median increment: 36 × 10^9/L
Levin, 2003[25]	No correlation between HLA antibodies by ELISA, LCT, LIFT + PIFT, and < 20% 1-hr recovery Positive ELISA and PIFT (p = 0.04) and LIFT + PIFT (p = 0.03) associated with 16-hr recovery <10%
Petz, 2000[16]	Mean 24-hr PPR: SDP, LR, HLA: 21 ± SEM 4%, p = ns vs. random SDPLR, CXM: 23 ± SEM 4%, p = 0.04 vs. random SDP, LR, ASP: 24 ± SEM 3%, p = 0.007 vs. random LR, SDP: 15 ± SEM 1%, p < 0.01 for ASP vs. random
Hogge, 1995[26]	11/16 (69%) with LCTABS had 2× CCI with HLA matched PLTs compared to RDP p < 0.01, 2/8 (25%) with no LCTABS had response to HLA-matched PLTs p = ns
Friedberg, 1994[27]	SPRCA CXM was better predictor than HLA for 1 hr, Median CCI ≥ 7.5 × 10^9/L for HLA CXM compatible vs. 0 for HLA CXM incompatible, p < 0.007, Mean CCI for HLA SDP: A + BU 6.1 × 10^9/L vs. BX + C 3.55 × 10^9/L vs. SDP, 0, p < 0
Moroff, 1992[45]	1-hr CCI ≥ 7.5 × 10^9/L, HLA 54% vs. CXM 48%, p = ns, 24-hr CCI ≥ 4.5 × 10^9/L, HLA 42%, CXM 23%, p < 0.05, 1-hr CCI A, BU 11.0 × 10^9/L vs. BX 6.0 × 10^9/L vs. C 9.0 × 10^9/L vs. D 8.0 × 10^9/L, p = ns, 1-hr CCI ≥ 7.5 × 10^9/L + 24-hr CCI ≥ 4.5 × 10^9/L in 53% of HLA-matched CXM compatible vs. 45% with HLA-matched CXM incompatible, p = ns
Bishop, 1988[46]	Mean 1-hr CCI: HLA antibody Grade 0, 15.5 × 10^9/L vs. Grade 1, 11.6 × 10^9/L; Grade 2, 8.9 × 10^9/L; Grade 3, 5.5 × 10^9/L; Grade 4 mismatch, 5.0 × 10^9/L
Murphy, 1987[28]	NR
Ware, 1985[29]	1- to 2-hr CCI HLA A match: 6,640 ± 7,290 HLA B match: 7,892 ± 6,857 HLA C match: 8,435 ± 9,820 HLA D match: 5,855 ± 9,027 Random: 18,415 ± 5,386
Dahlke, 1984[30]	CCI from HLA A3 mismatch to A1 or A11 vs. A- and BU-matched PLTs was less, p < 0.001, A1 or A11 mismatched to A3 vs. A and BU associated with small increments p < 0.001, In B5 group B18, BW16 higher CCI (p < 0.01), Lower CCI with B7 and BW21 Low CCI with B5 to B15 and B17 (p < 0.01), Low CCI B27 to B7 (p < 0.01) and with B8 and B14 bidirectionally and B12 and BW21 bidirectionally (p < 0.05)
Hester, 1978[31]	Median 1-hr CCI for afebrile patients with two antigens shared = 12.0 × 10^9/L vs. 8.0 × 10^9/L for febrile patients (p = 0.01) Median 1-hr CCI for patients with two antigens shared = 12.0 × 10^9/L vs. ≤8.0 × 10^9/L in patients with one antigen, no antigen, or unknown (p < 0.01) No difference of CCI for one antigen match vs. no antigen match Median CCI related to number of antigens shared and not specific antigen of haplotype
Macpherson, 1979[32]	CCI > 5.0 × 10^9/L in 40% HLA A match vs. 55% in BX p = ns, vs. 14% in C p < 0.05, vs. 21% in D
Duquesnoy, 1977[13,21]	1- and 24-hr recovery 55%-75% and 40% for HLA A and B, HLA C and D recovery less than A and B (p < 0.001), 51% responded to HLA C and D PLTs 24-hr % increment by LCT for HLA A2 positive 40% vs. HLA negative 52% with A1, B1U, and B2U, p = 0.1, 25% vs. 53%, p = 0.003 with B1X, B2UX, B2X, 9% vs. 36% with C, D, p = 0.0009
Wu, 1977[33]	1-hr CCI ≥ 10.0 × 10^9/L and/or 20 hr ≥8.0 × 10^9/L in 2/4 (50%) HLA A vs. 0/1 B1 vs. 1/1 (100%) B2 vs. 1/2 (50%) C vs. 10/19 D for related PLTs, 1/1 (100%) HLA C vs. 6/13 HLA D for unrelated
Herzig, 1975[34]	44%-72% of HLA matched tx had 20 hr CCI > 4.5 × 10^9/L vs. 72%-96% with HLA LR, p < 0.05. Median duration of response 3.5 months for RDP vs. >6 months for LR p < 0.02, HLA-A and B1 4.5 months vs. B-2 and C 1.5 months p < 0.01, duration has not been reached if LR HLA used and no difference between HLA-A and B-1 vs. B-2 and C

TABLE 4. *Continued*

Author, year	PLT count increment
Retrospective	
Fontaine, 2011[35]	Mean 1-hr CCI range: 3.4 × 10^9 to 28 × 10^9/L 16.4 × $10^9$for C1 q compatible, IgG compatible 10.6 × 10^9, for C1q compatible, IgG incompatible 2.5 × 10^9, for C1q incompatible, IgG incompatible Number of adequate PLT transfusion: 90% IgG compatible, C1q compatible 62% IgG incompatible, C1q compatible 14% IgG incompatible, C1q incompatible p < 0.0001
Pai, 2010[22]	Retrospective study: the 24 CCI and CCI > 4.5/L for CREG, A/BU matched and EBM equivalent and greater than SDP Prospective study: median CCI for A/BU 14.6 (10.5-22.2) vs. CREG, 10.1 (2.1-26.3) vs. EBM 22.03 (9.9-30.9) p = 0.034 (for EBM vs. CREG) Successful tx in 85% A/Bu vs. 63% CREG vs. 84% EBM, p = 0.004 for EBM vs. CREG
Brooks, 2008[47]	Median 1-hr CCI with TMMs ≤ 9 8.0 × 10^9/L vs. TMMs > 9 6.0 × 10^9/L (p < 0.01) Median 1-hr CCI with EMMs ≤ 11 7954 × 10^6/L vs. EMMs > 11 6356 × 10^6/L (p = 0.02) No difference for 24-hr CCI
Nambiar, 2006[17]	Median 15-min to 1-hr CCI for TMMs ≤ 9, 13.5 vs. TMMs> 9, 11.2 (p < 0.01), AUC for TMMs 0.62 and 0.63 for HIMMs, Median CCI 14.0 × 10^9/L for HIMMs ≤ 3 vs. 11.2 × 10^9/L for HIMMs >3, p < 0.01, 13.5 × 10^9/L TMMs ≤ 9 vs. 11.2 × 10^9/L TMMs > 9, p < 0.01
Levin, 2004[36]	1-hr recovery—47% in patients with positive HLA antibody tests vs. 35% for patients with negative test (p = 0.04), 16-hr recovery—34% with positive HLA antibody tests vs. 15% with negative test (p = 0.03)
McFarland, 1989[37]	Correlation between PLT recovery at 1 hr and HLA match grade: median A vs. B1-B2 (p < 0.05), vs. B3-B4 (p < 0.001), vs. C (p < 0.005), vs. D (p < 0.005) Median B1-B2 vs. B3-B4 (p < 0.02), vs. D (p < 0.07) Correlation between PLT recovery at 18-24 hr and HLA-match grade: median A vs. B1-B2 (p < 0.03), vs. B3-B4 (p < 0.001), vs. C (p < 0.001), vs. D (p < 0.0001) Median B1-B2 vs. B3-B4 (p < 0.05), vs. D (p < 0.02) The effect of HLA seen only when LCT > 20%, clinical factors more important than HLA for 1-hr recovery and vice versa for 24-hr recovery by regression analysis
Heal, 1987[38]	CCI ≥ 7.5 × 10^9/L 33% for CXM+, 57% for CXM– (p < 0.01), A/BU 74%, BX 62%, C 51%, p = 0.03 for A/BU vs. C CXM most significant predictor of CCI vs. HLA and ABO, p = 0.002, HLA > ABO, p = 0.02
Klingemann, 1987[39]	5/71 (7%) refractory patients did not respond to HLA-matched PLTs
Levy, 1984[40]	Mean increment 33.0 × 10^9/L with HLA-matched PLTs
McElligott, 1982[41]	1-hr recovery for HLA Bw4/Bw6 compatible 84% vs. incompatible 52%, p < 0.02 24-hr recovery for compatible 44% vs. incompatible 24%, p < 0.01
Daly, 1980[42]	For refractory patients (CCI < 10.0 × 10^9/L at 1 hr) CCI at 1 hr were 15.0 × 10^9/L with HLA-matched vs. 3.0 × 10^9/L with RDP (p < 0.001), For refractory patients (CCI<10.0 × 109/L at 1 hr) CCI at 18 hr were 9.0 × 10^9/L with HLA matched vs. 1.0 × 10^9/L with RDP (p < 0.001), For nonrefractory patients (CCI ≥ 10.0 × 10^9/L at 1 hr) CCI at 1 hr were 12 (5-22) with HLA matched vs. 13 (10-20) with RDP (p value NR), For nonrefractory patients (CCI ≥ 10.0 × 10^9/L at 1 hr) CCI at 18 hr were 4.0 × 10^9/L with HLA-matched vs. 3.0 × 10^9/L with RDP (p value NR)
Tosato, 1978[12]	12-20 hr CCI > 5.0 × 10^9/L HLA-A 61% vs. B1 41% vs. B2 49% vs. C 42% vs. D 43% (p < 0.04 for A vs. B1, B2, C, D)
Mittal, 1976[43]	PPR 44%-49% for matched vs. 15% unmatched, p < 0.001
Lohrmann, 1974[44]	Median 1-hr CCI: HLA A 15.0 × 10^9/L vs. B1 14.7 × 10^9/L, p = ns vs. B2 6.3 × 10^9/L, p < 0.001, B1 vs. B2, p < 0.001 Median 20-hr CCI: HLA A 12.5 × 10^9/L vs. B1 10.9 × 10^9/L p = ns, vs. B2 4.8 × 10^9/L, p < 0.001 vs. mismatch, p < 0.001, B1 vs. B2, p < 0.005, B1 vs. mismatch, p < 0.001, B2 vs. mismatch, p < 0.001

ASP – HLA antibody specificity prediction method; C1q – first complement component; CXM – crossmatch; EBM – epitope-based match; ELISA – enzyme-linked immunosorbent assay; EMMs – epiot amino acid mismatches; HIMMs – highly immunogenic mismatches; IgG – immunoglobulin G; IR – irradiated; LCT – lymphocytotoxicity assay; LCTABS – lymphocytotoxic antibodies; LIFT – lymphocyte immunofluorescence test; LR – leukoreduced; ns – not significant; NR – not reported; PIFT – PLT immunofluorescence test; PPR – percentage of PLT recovery; RDP – random-donor pooled PLTs; SDP – single-donor PLTs; SPRCA – solid-phase red blood cell adherence.

Quelle prise en charge ?

Transfusion de CPA HLA compatible : gold standard dans la prise en charge des ER :

- CPA HLA >> CPA random ou MCP
- Les anticorps HLA sont responsables de l'ER immunologique (MFI+)
- Efficacité démontrée

Allemagne

2.8.3 Selection of compatible platelet concentrates in immunized patients

In patients with confirmed class-I HLA alloantibodies HLA-well-matched compatible platelets should be used for transfusion after verification in a cross-match procedure [14, 40, 53]. In broadly immunized patients (reactivity with more than 80–90 % of the test cells) it is recommended to determine HLA-A and HLA-B antigens of the patient in order to be able to preselect potentially suitable platelet donors (→ apheresis platelet concentrates). HLA- and HPA-compatible donors should be selected for patients who have formed HPA antibodies in addition to HLA class I antibodies [37].
Transfusion outcome should be controlled by determining platelet increment in order to detect additional immunization at an early stage. For this purpose platelet counts are determined prior to transfusion and 1 hour and approx. 20 hours post transfusion. The corrected count increment (CCI) represents a "normalized" measure [10].

CCI = (platelet increment per µL × body surface in m^2)/number of platelets transfused (× 10^{11})

In case of refractoriness corrected increments determined after 1 hour are <7,500, and values determined after 20 hours <4,500.

Regarding management of the refractory patient, it is recommended:	
in patients with confirmed HLA class I antibodies to transfuse HLA-compatible platelets obtained by apheresis.	**1 B**
to transfuse HLA- and HPA-compatible platelets obtained by apheresis in patients who have also formed HPA antibodies.	**2 C**
to control transfusion outcome in immunized patients by determining corrected count increment	**2 C**

Royaume Uni

Recommendations for Platelet Refractoriness:

- **ABO matched platelets should be used when available to maximise increments (2C)**
- **Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions solely due to non-immune factors should not receive HLA-selected platelet transfusion (2C)**
- **Patients with hypoproliferative thrombocytopenia who are refractory to platelet transfusions and have class I HLA antibodies should receive class I HLA-selected platelet transfusion (Harris *et al*, 2009) (2C)**
- **Patients with hypoproliferative thrombocytopenia who continue to be refractory to HLA-selected platelet transfusions and have human platelet antigen (HPA) antibodies should receive HPA-selected platelet transfusion (2C)**
- **Patients with hypoproliferative thrombocytopenia who are not refractory to platelet transfusion should not receive HLA-selected or HPA-selected platelets (2C).**

Australie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Original Article

Human leukocyte antigen sensitization from red cell transfusions: Rate and risk factors in renal and nonrenal patients requiring transfusion

7 September 2025

Jeremy S. McComish[1,*], Jessica Brewster[1], Emma Carreiro[1], Kevin Chow[2,3], Christopher Hogan[4], John Kanellis[5], Darren Lee[6,7], Sanjoy Paul[8], John Whitlam[7], Daniela Zantomio[4], James Daly[1]

Problème de disponibilité de donneur lié à une hyperimmunisation

Quelles alternatives ?

Rituximab, daratumumab, bortezomib

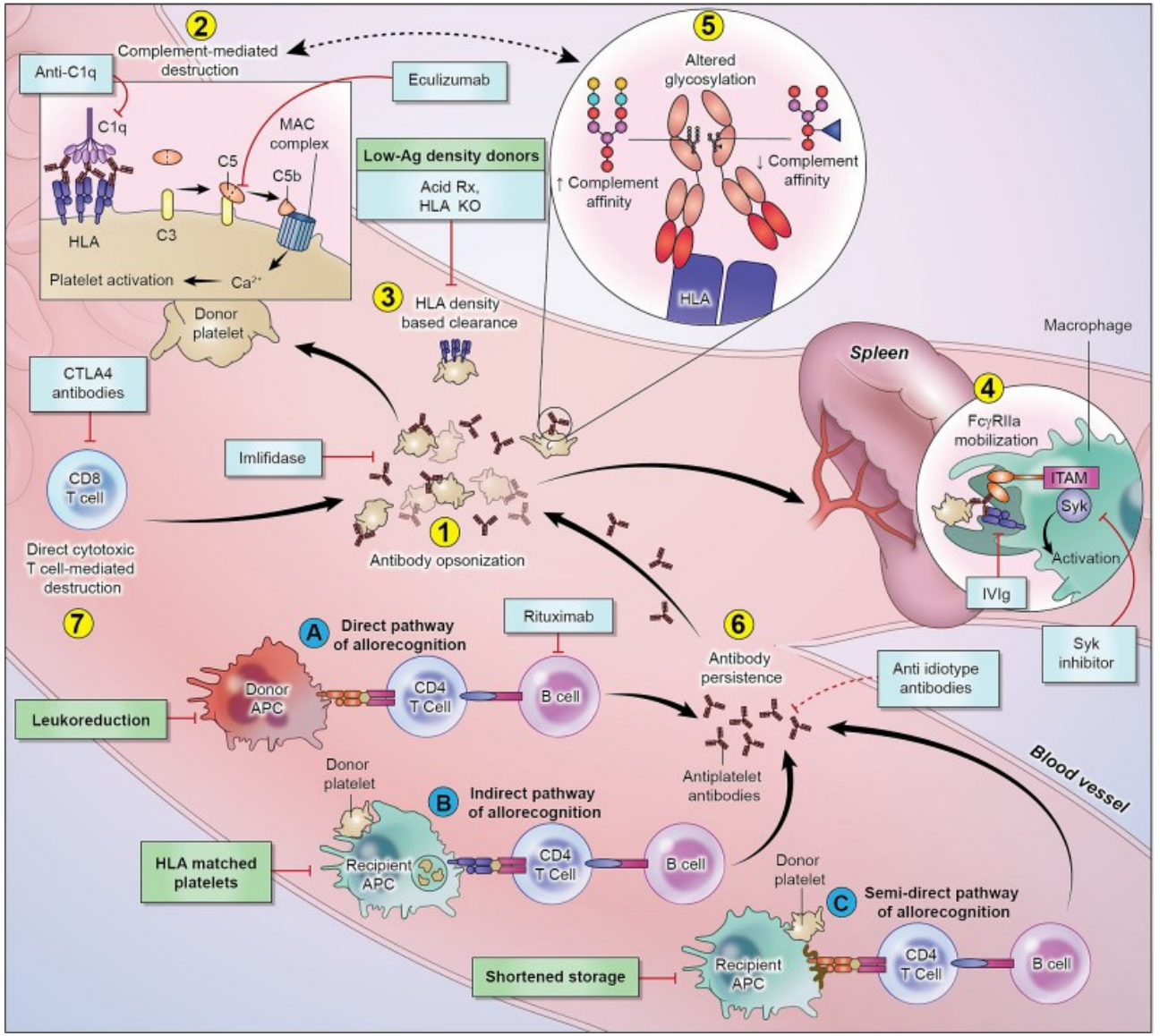
Miki H, et al. Int J Hematol (2009)
Liu W, et al. Int J Clin Exp Med (2015)
Yu Q-H, et al. Platelets (2015)

Anti-complément : l'éculizumab

Vo P, Purev E, et al. Br J Haematol (2020)

IdeS : Imlifidase

Qamar et al., Blood (2022)
Lynch et al. Blood Advances (2022)



Quelles alternatives ?

Place des échanges plasmatiques ?

1. Bensinger WI, et al. Transplantation. 1986
2. Murphy MF, et al. Blood Rev. 1990
3. Buskard N, et al. Transfus Sci. 1998
4. von Baeyer H, et al. Ther Apher Dial. 2003
5. Finn L, et al. Transfusion and Apheresis Science. 2013
6. Cid J, et al. Platelets. 2015
7. Cuker A, et al. Blood. 2016
8. Padmanabhan A, et al. Journal of Clinical Apheresis. 2019
9. Pedini P, et al. Transfusion. 2022
10. Raza S, et al. Transfusion and Apheresis Science. 2023
11. Thomas J, et al. Clin Case Rep. 2026.

+ cas dans les centres experts

Vieilles publications
Cas cliniques
Urgences hémorragiques
Dernière ligne : pas de donneur compatible
Pas de recommandations fortes

Mais efficacité de certaines stratégies

Quelles alternatives ?

Merci au Dr Guillaume DAUTIN

Patiente de 54 ans : asthénie et épistaxis modérés fréquents

Clinique :

- Apyrétique
- Absence de syndrome tumoral
- Absence d'hépatosplénomégalie
- Pas d'anomalie cardio-pulmonaire

Bilan sanguin :

- Biochimie, enzymologie, hémostase, bilan inflammatoire : normal
- NFS :
  - ☐ Leucopénie : 1000/mm3
  - ☐ Polynucléaire neutrophile < 10%
  - ☐ Anémie: Hb : 8g /100 mL, GR normaux
  - ○ Thrombopénie sévère : plaquettes : 1G/L
- Myélogramme :
  - ○ Moelle pauvre en cellules
  - ○ Absence de mégacaryocyte

Diagnostic

➢ Hypoplasie médullaire avec absence de mégacaryocyte

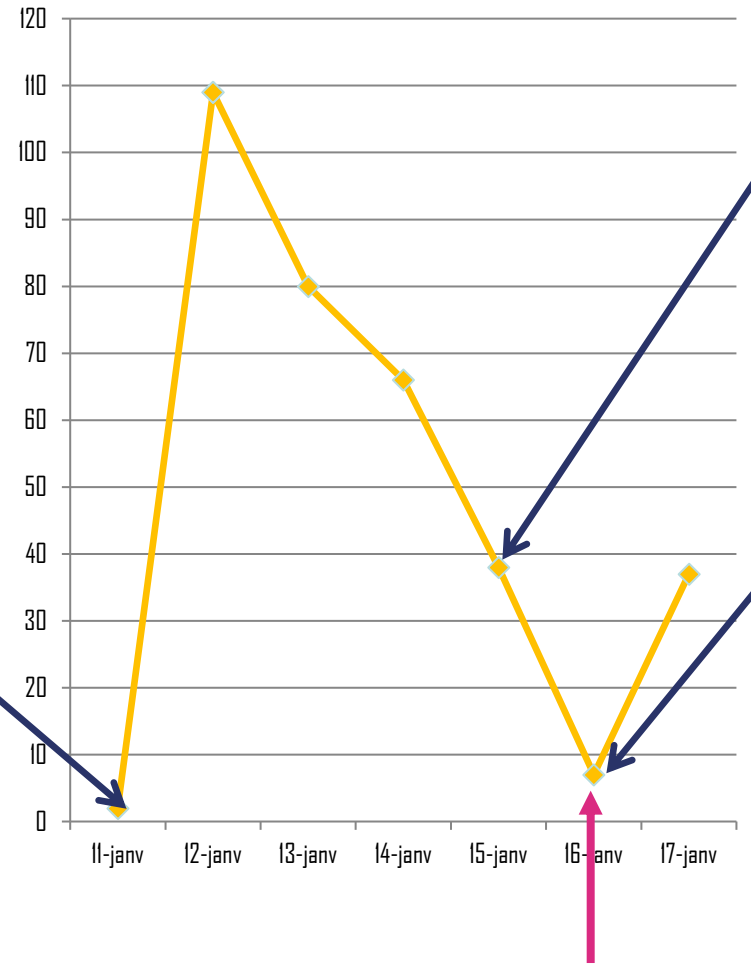
Traitement

➢ Traitement de l'hypoplasie médullaire:

➢ **Thrombopénie :**
  - ○ **Transfusion de plaquettes**
  - ○ **Mesure de l'efficacité de la transfusion**

Quelles alternatives ?

1ère transfusion
CPA
CCI = 36

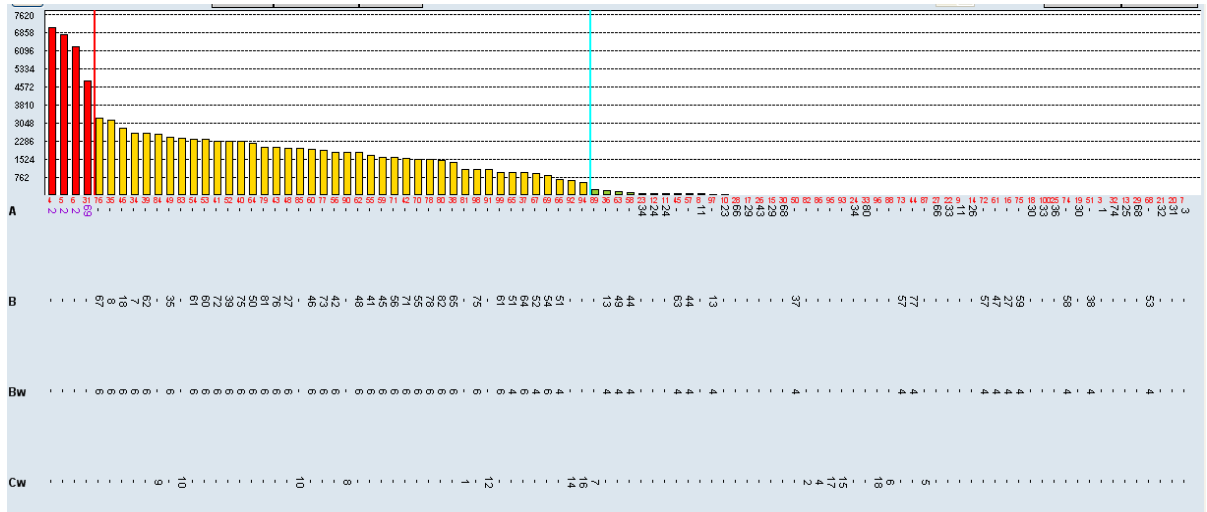


2ème transfusion
MCPS
CCI = **-12**

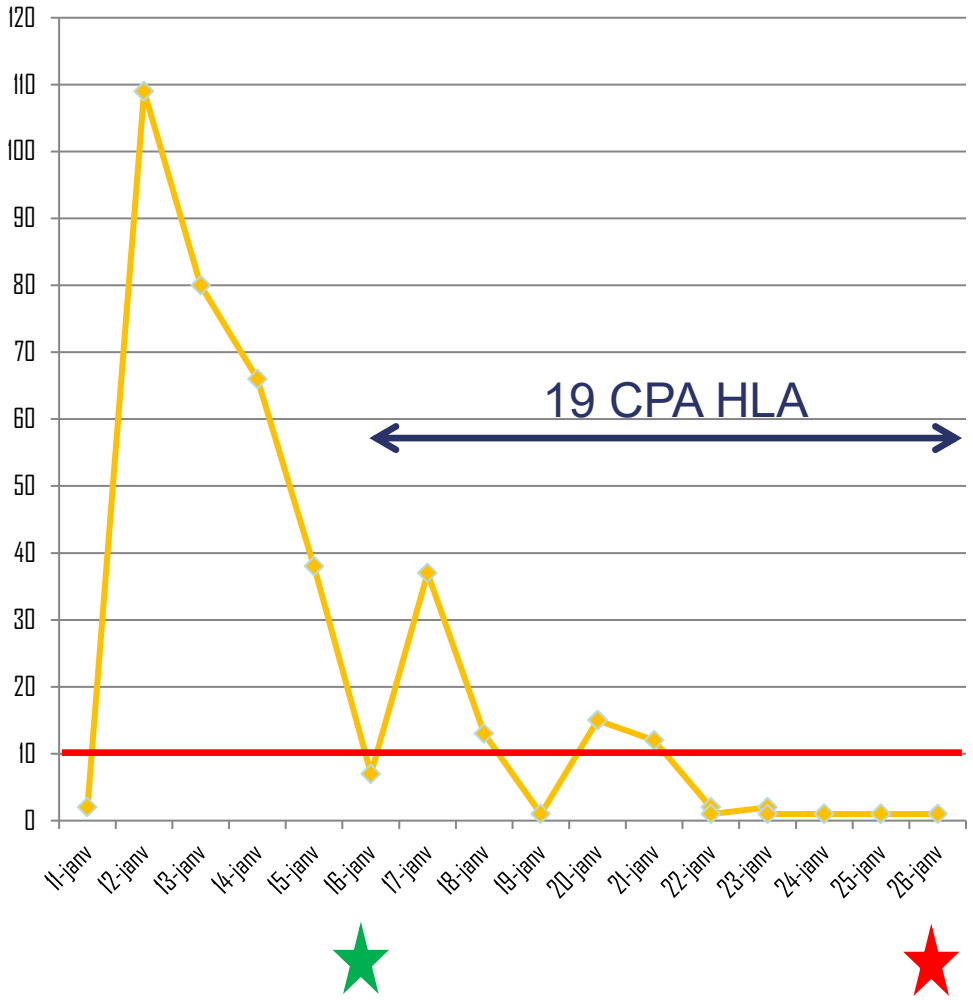
3ème transfusion
CPA HLA compatible
CCI = 13

Immunisation anti-HLA
Consigne transfusionnelle
CPA HLA compatible

Retour à l'efficacité transfusionnelle

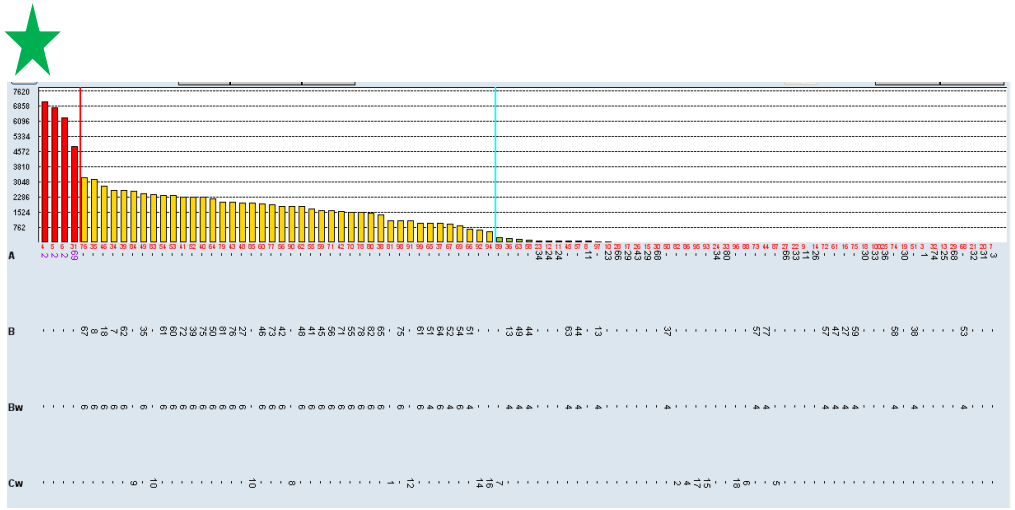


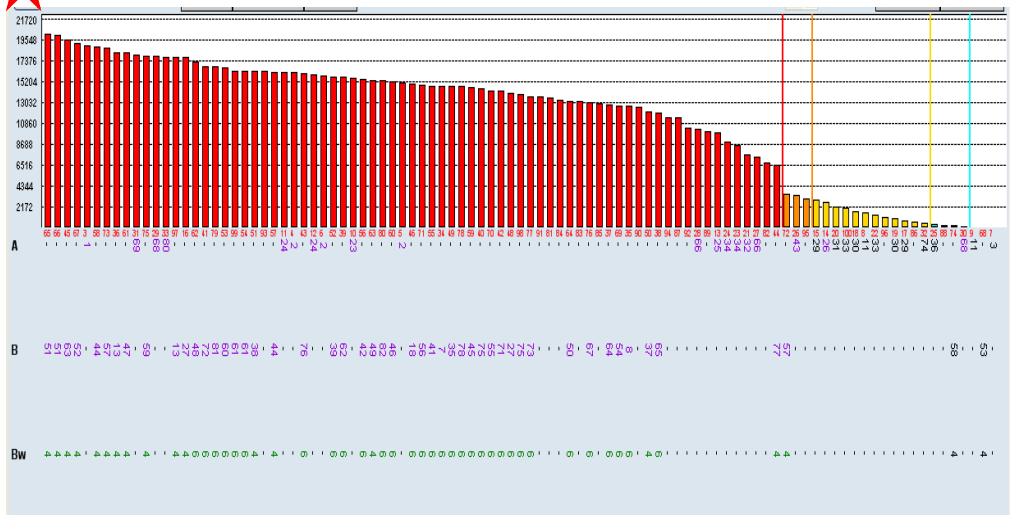
Quelles alternatives ?



16/01 :
consigne transfusionnelle

26/01 :
nouvelle étude du profil





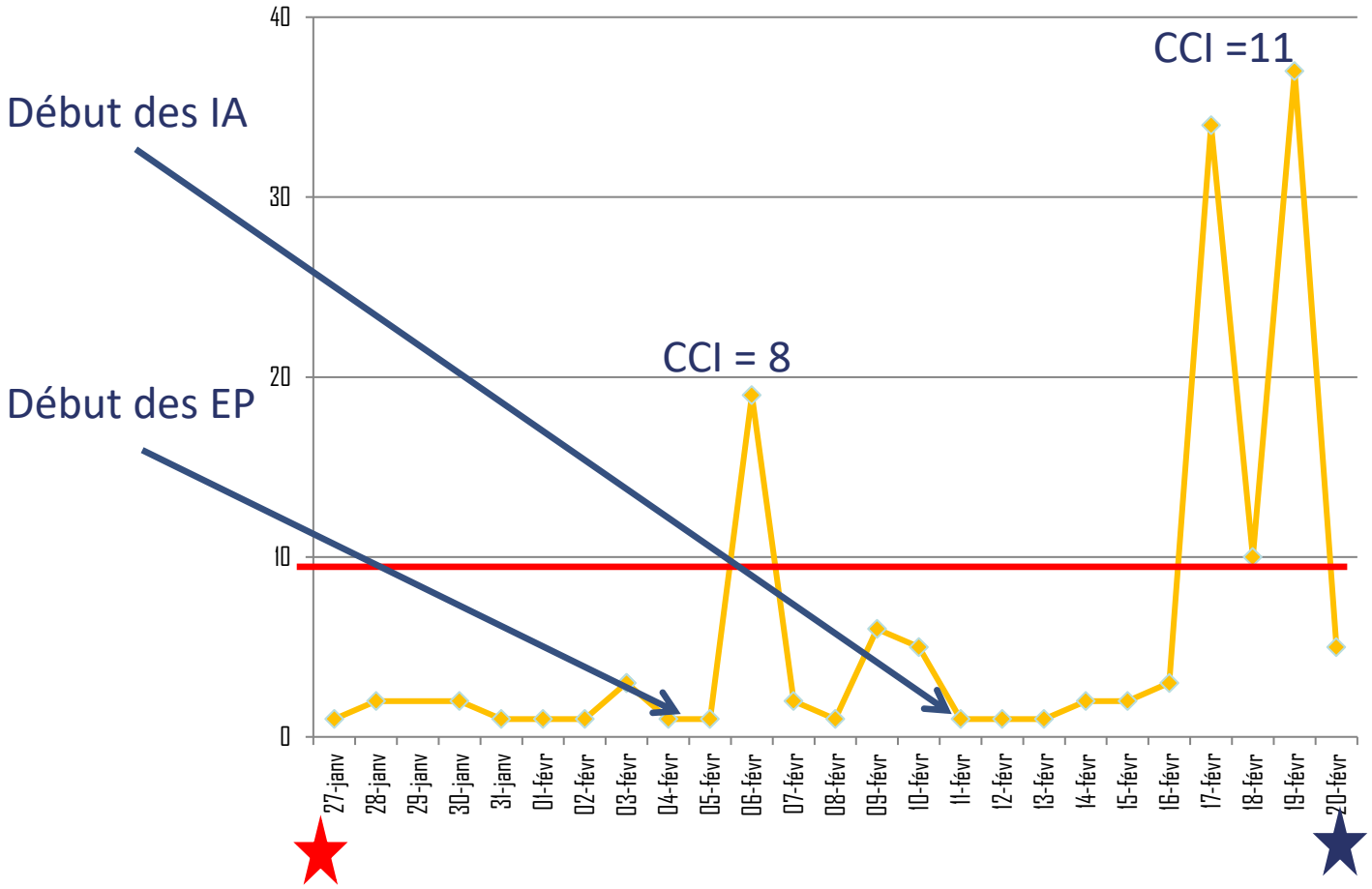
Quelles alternatives ?

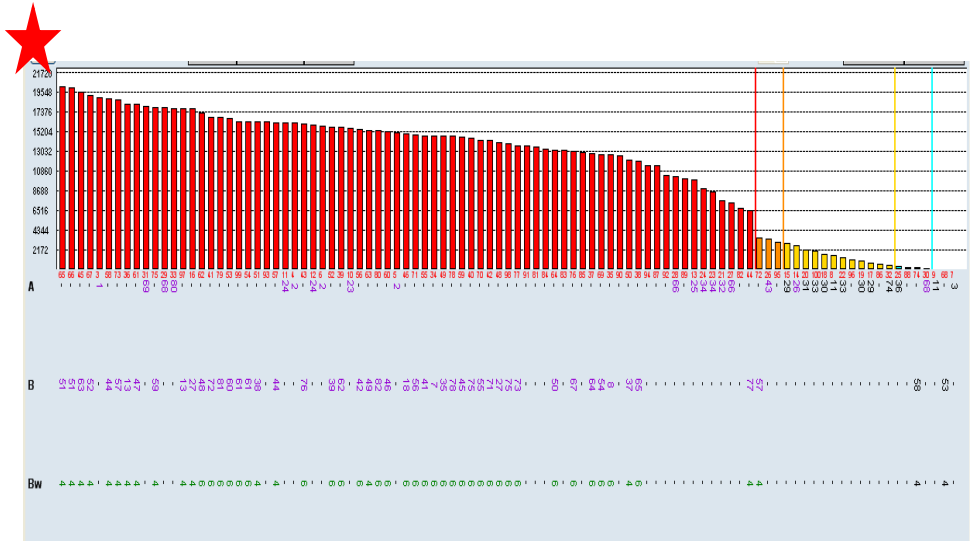
- Grandes difficultés de transfusion :
  - Patiente hyper-immunisée anti-HLA
  - **Pas de donneur HLA compatible en France**
- Etat clinique de la patiente :
  - Signes hémorragiques sévères (cutanés, gingivaux)
  - Risque d'hémorragie méningée fatale +++
  - Pronostic vital engagé

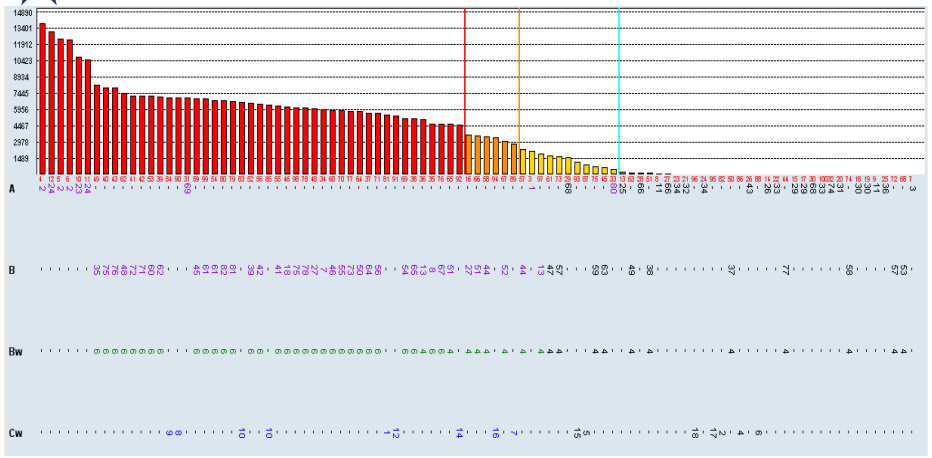
- Intensification thérapeutique :
  - Thrombopénie :
    - Transfusions quotidiennes avec MCPS
    - Facteurs de croissance plaquettaire (Nplate® puis Révolade®)
  - Immunologie :
    - Immunosuppression : ciclosporine, corticoïde +++, Rituximab®
    - Immunoglobulines en IV

Inefficace

Quelles alternatives ?



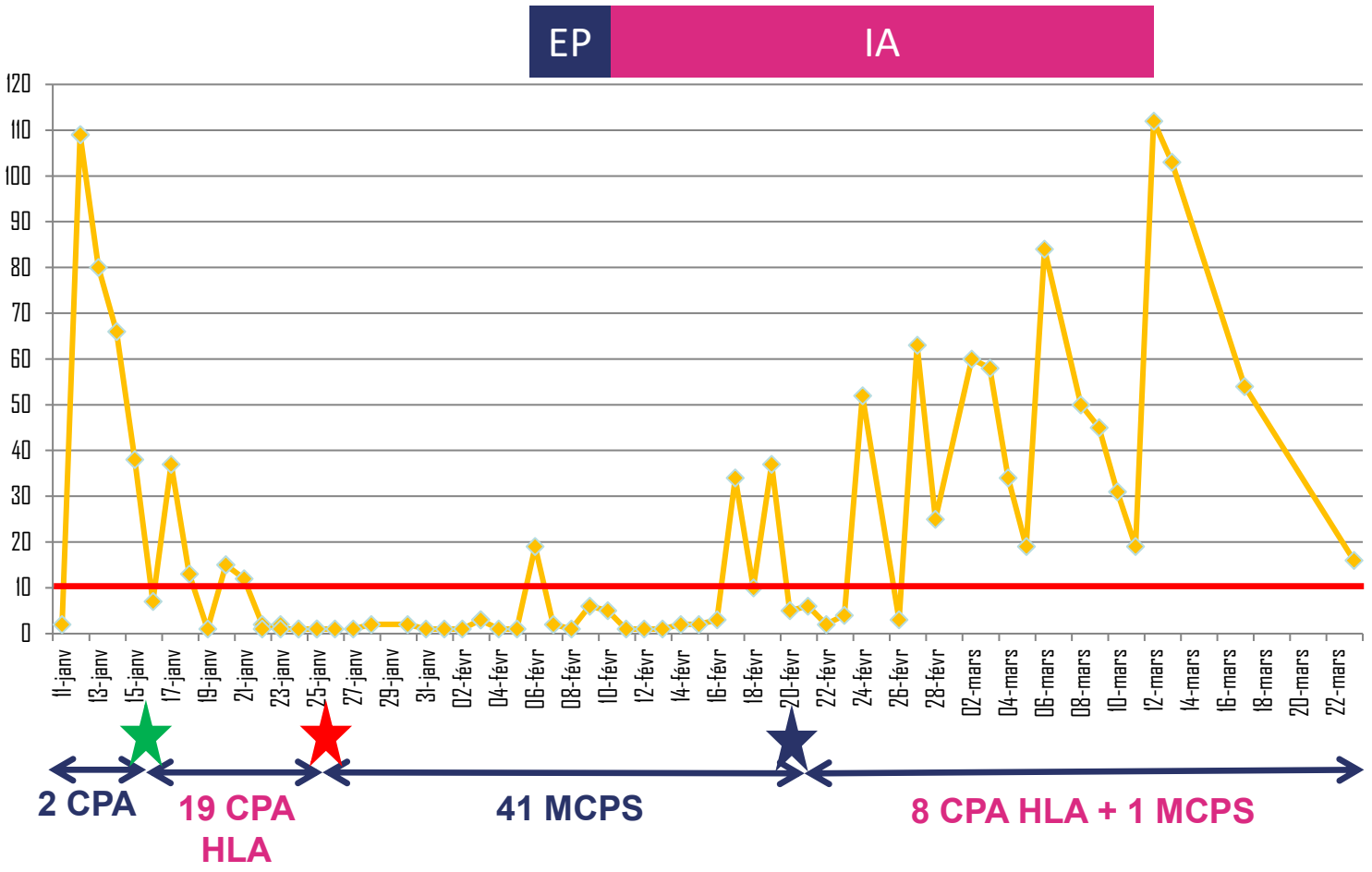




Baisse significative du profil d'allo-immunisation anti-HLA

Convocation possible de donneurs de plaquettes spécifiques

Quelles alternatives ?



Quelles alternatives ?

Conclusion :

- Efficacité de la stratégie de desimmunisation
- Permet de diminuer les titres et les spécificités anti HLA
- Permet de trouver des donneurs de CPA HLA compatible

Quelles alternatives ?

TRANSFUSION

A case of platelet transfusion refractoriness in a CD36-negative patient with acute myeloid leukemia: Diagnostic and therapeutic management

Pascal Pedini [1 2], Yosr Hicheri [3], Gerald Bertand [4], Isabelle Dettori [1], Agnes Basire [1], Catherine Lazaygues [1], Corinne Chabrières [1], Camille Perrin [1], Jeanne Pascal [1], Jacques Chiaroni [1 2], Virginie Renac [4], Patrick Ladaique [3], Norbert Vey [3 5], Christophe Picard [1 2]

Glycoprotéine transmembranaire à la surface des **plaquettes**, des **monocytes**/macrophages, des érythroblastes, des cellules endothéliales *(Greenwalt, 1992),* des cardiomyocytes, des adipocytes *(Hirano, 2003),* et des **érythrocytes** (Alattar, 2024)

Fréquence phénotype CD36 NEG :

- **Caucasiens <0,3%**
- Africains 2,5-7%
- Asiatiques 3-11%
- Péninsule arabique 2,6%

→ **Risque d'iso-immunisation anti-CD36**

Donneur de plaquettes CD36 NEG extrêmement rare

Quelles alternatives ?

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1. **Trouver un donneur CD36-** : 334 donneurs d'ancestralité africaine contactés => 27 testés => **1 CD36-**
2. **2 poches de plaquettes autologues** ont pu être prélevées avant la seconde consolidation
3. **Protocole de désensibilisation** (Rituximab + Bortezomib + EP)

TABLE 1 Transfusion effectiveness

Chemotherapy course	Product	ABO group	Date of transfusion	Platelet numeration before transfusion (G/L)	Platelet numeration after 24 h transfusion (G/L)	Platelet dose transfused (10^{11})	24 h CCI
Induction	Apheresis	O	0	17	32	3.66	7.03
	BCP	O	4	8	19	3.2	5.9
	BCP	O	5	3	3	4	0
	BCP	O	6	3	3	5.7	0
	BCP	O	7	3	3	6.8	0
	BCP	O	8	3	3	7	0
	BCP	O	9	3	3	3.7	0
First consolidation	BCP	O	39	14	9	7.2	−1.19
	BCP	O	40	9	7	6.5	−0.53
Second consolidation	Apheresis[£]	O	104	11	63	4.93	18.1

TABLE 2 Monitoring (MFI) of CD36 antibodies by Luminex in the desensitizing protocol (positive cut-off MFI value >1000)

	Therapeutic setting	Day after first transfusion	Serum undiluted (MFI)	Serum dilution (MFI)					
				1/10	1/50	1/100	1/200	1/400	1/500
Desensitization	Diagnosis	6	5,326						
	Rituximab	83	6,335	4,025	2,072	1,089	856		218
	Before PP	87	7,015		5,351	4,046	1,768	1,073	
	After PP	87	5,144		2,755	1,557	682	348	
	Bortezomib	89	12,727		4,269	2,869	1,443	687	
	After PP	90	9,418		1,925	914	446	192	
Follow-up		93	9,839		3,187	1,812	692	356	
		102	10,075		3,114	2,124	1,269	613	
		138	9,335		3,189	1,724	1,105	456	318

➡ Efficacité de la transfusion avec CPA CD36-

➡ Peu d'efficacité de désensibilisation

Quelles alternatives ?

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- **Pas d'efficacité des échanges plasmatiques**
- **Pas d'alloimmunisation anti HLA mais isoimmunisation anti CD36**

Quelles alternatives ?

TABLE 10. *Outcome of plasmapheresis in alloimmune thrombocytopenia*

Syndrome	Reference	Number of patients (*n*)	Type of plasmapheresis	Response (sustained) (*n*)
Alloimmune thrombocytopenia				
RTP	(62)	10*	PA	6
PTP	(65)	3	PEX/HA	2
	(66)	1	PAI	1
	(64)	1	PEX/HA	1
Post-TP AITP	(48)	3	IA	0

*Nine cases did not respond to IVIg or glucocorticoids; TP, transplant; RTP, refractoriness to platelet transfusion; PTP, post-tranfusion purpura.

*The data seem to **confirm a real therapeutic benefit** of plasmapheresis in RTP and PTP, but an independent expert opinion is lacking. Hence, **the indication for plasmapheresis is classified as experimental** in both syndromes.*

Quelles perspectives ?

Ingénierie cellulaire

Plaquettes universelles HLA-I deplétées par traitement à l'acide

Mirlashari MR, et al. Transfusion (2021)
Mirlashari MR, et al. Transfus Med (2023)

→ Prometteur dans modèle murin

Plaquettes de culture (IPS) : iPLAT1

iPLAT1: the first-in-human clinical trial of iPSC-derived platelets as a phase 1 autologous transfusion study

Sugimoto N, et al. Blood (2022)

→ Essai clinique chez l'humain

Plaquettes universelles allogénique (β2 microglobulin knockouts)

Generation of HLA Universal Megakaryocytes and Platelets by Genetic Engineering

Figueiredo, C. & Blasczyk, Front. Immunol. (2021)

→ Preuve de concept

Conclusion

Gestion des thrombopénies réfractaires et transfusion plaquettaire

- **L'état réfractaire plaquettaire est souvent multifactoriel**, majoritairement non immunologique.
- Le CCI à 1 h et 24 h est central pour orienter le diagnostic et la prise en charge
- **Les anticorps anti-HLA** sont la principale cause des formes immunologiques
- **Les CPA HLA compatibles constituent le gold standard** chez les patients immunisés en ER
- En situation **de difficulté transfusionnelle**, des stratégies alternatives ciblées peuvent **restaurer transitoirement l'efficacité**
- L'hémaphérèse peut **être discuté dans ce cadre** **(sans niveau de preuve satisfaisante pour en faire une recommandation) :**

➡ **Rôle de l'immunisation ? Anticorps ? Intensité ?**

Conclusion

LBMR Gestion des thrombopénies réfractaires et transfusion plaquettaire

EFS Rennes

EFS Créteil

EFS Lyon Décines

EFS Marseille

Gestion des thrombopénies réfractaires et transfusion plaquettaire

Merci

Merci au Dr Guillaume Dautin