Acquired SAA: place of immunosuppression and TPO recetor agonists in 2022

Régis Peffault de Latour, MD, PhD

French reference center for aplastic anemia & PNH
French network for rare immunological & hematological disorders (MaRIH)
Severe aplastic anemia working party of EBMT (SAAWP EBMT)
Hôpital Saint-Louis, Paris, France

MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

APLASIE MEDULLAIRE
centre de référence

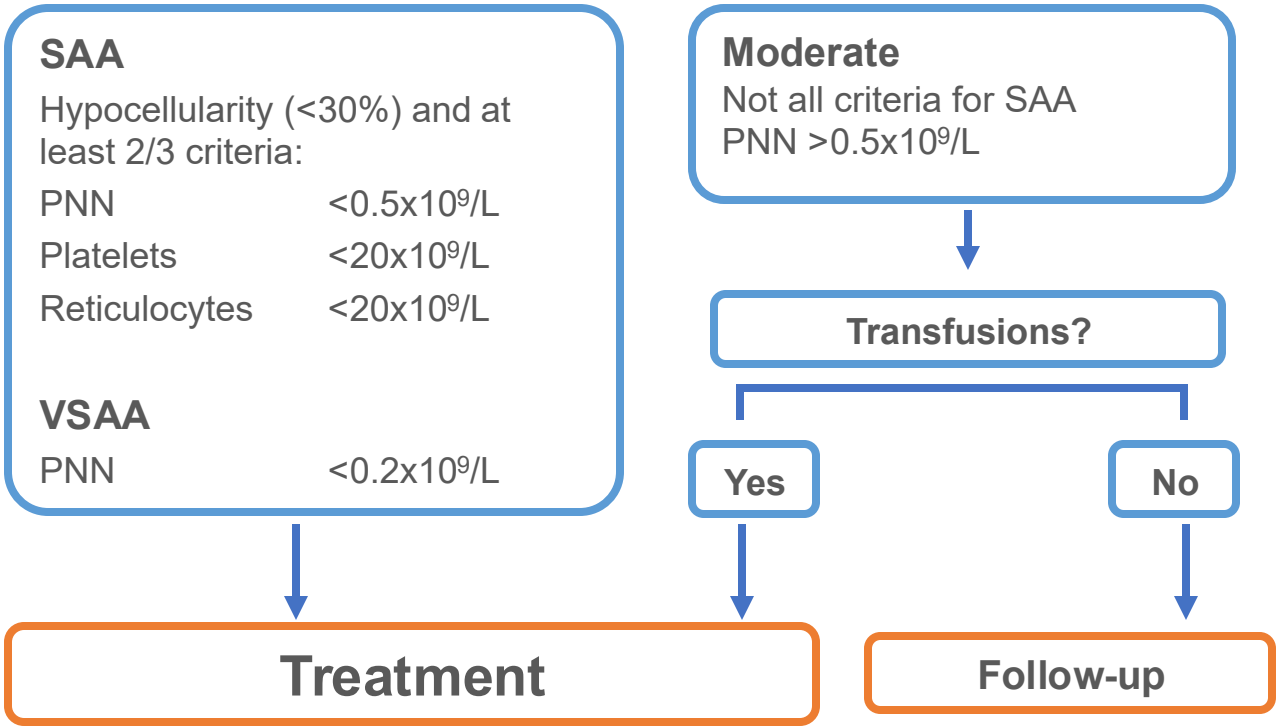
Disclosures

- **Expert consultant / speaker:** Alexion, Amgen, Apellis, Jazz, Novartis, Pfizer, Roche & Samsung
- **Research grant:** Alexion, Novartis & Pfizer

Patient case

- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

When should we start a treatment?



SAA, severe AA; VSAA, very severe AA.
Camitta BM, et al. Blood. 1976;48:63–70.

Patient case

- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

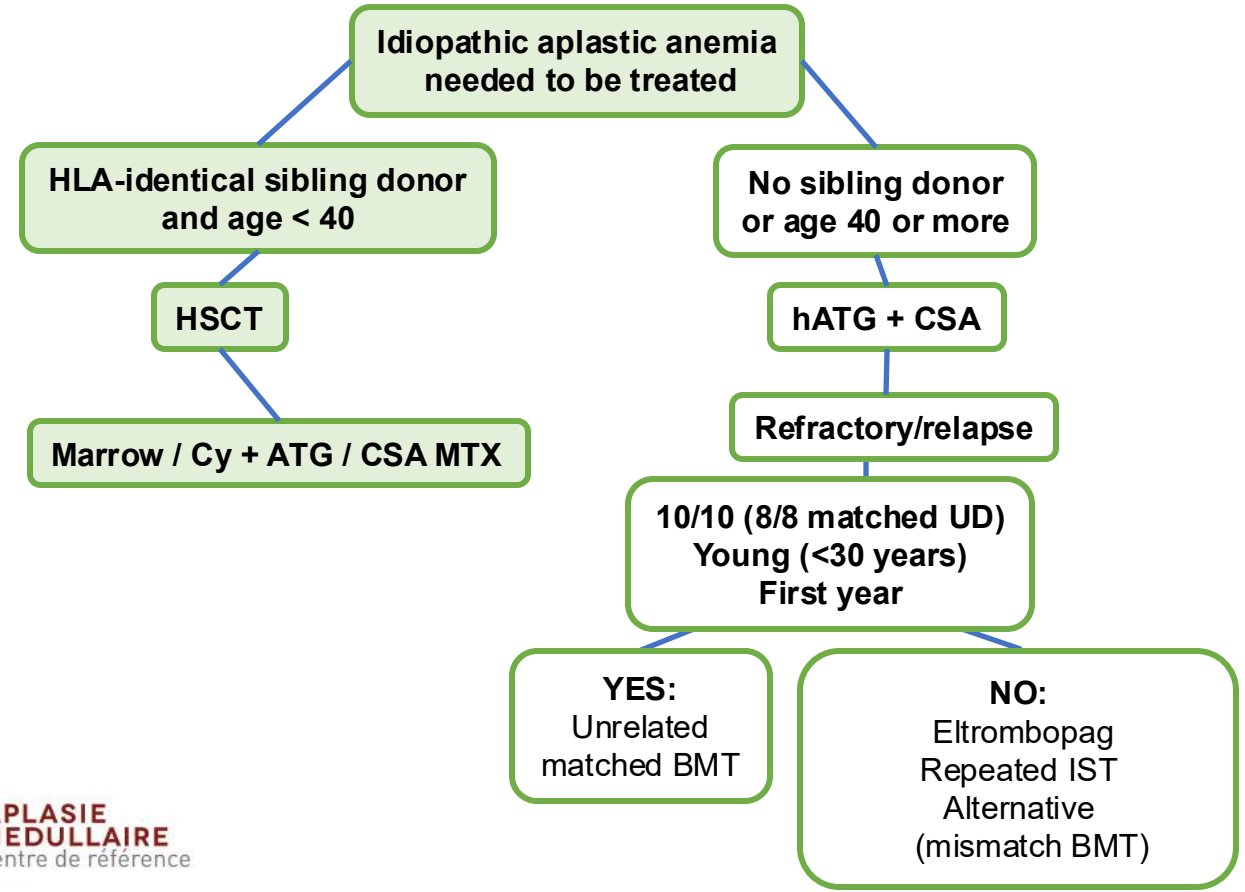
1 sibling available

MaRIH

APLASIE MEDULLAIRE centre de référence

Treatment (guidelines)

Cf Andrea Bacigalupo



MaRIH

APLASIE MEDULLAIRE centre de référence

Patient case

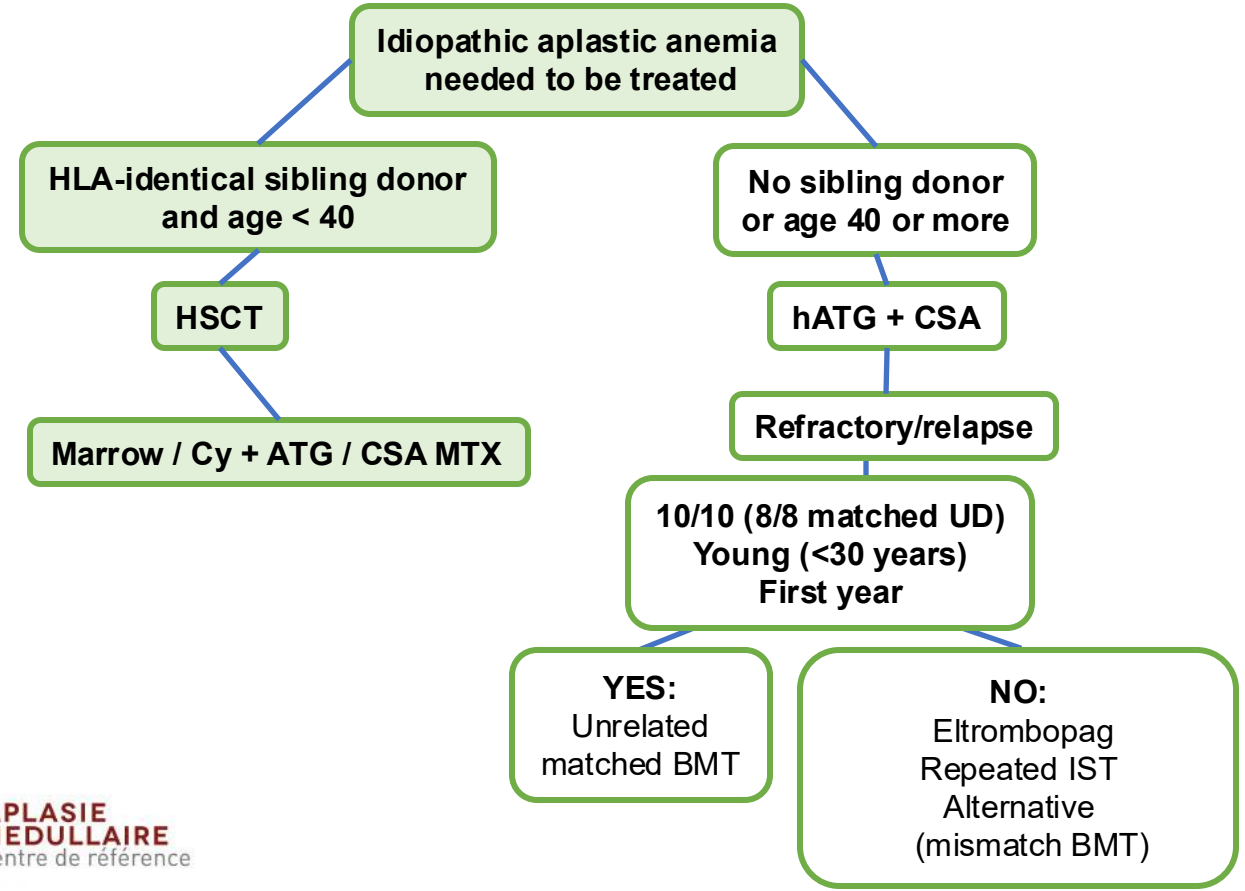
- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

No sibling but good probability for a 10/10 unrelated donor

MaRIH

APLASIE MEDULLAIRE centre de référence

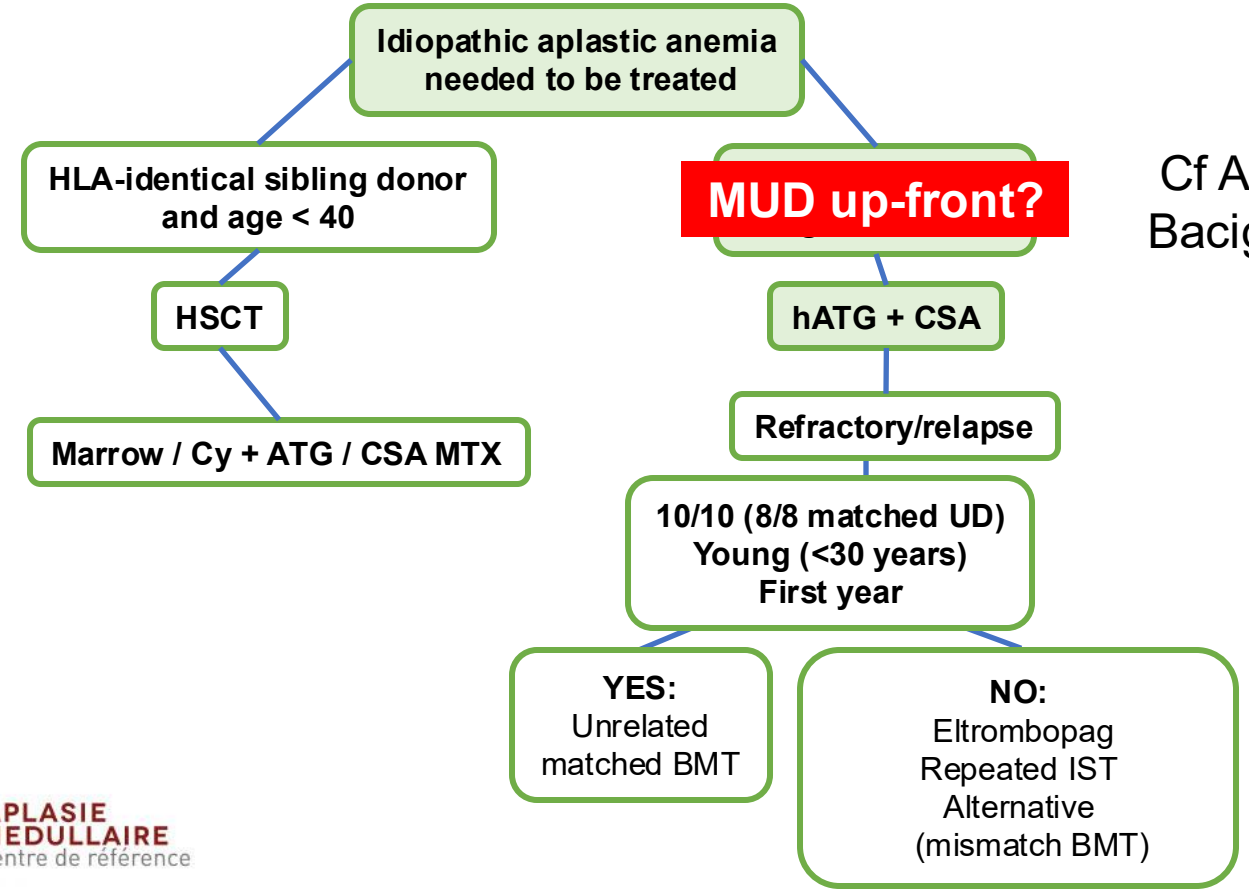
Treatment (guidelines)



MaRIH

APLASIE MEDULLAIRE centre de référence

Treatment (guidelines)



Cf Andrea Bacigalupo

MaRIH

APLASIE MEDULLAIRE centre de référence

Patient case

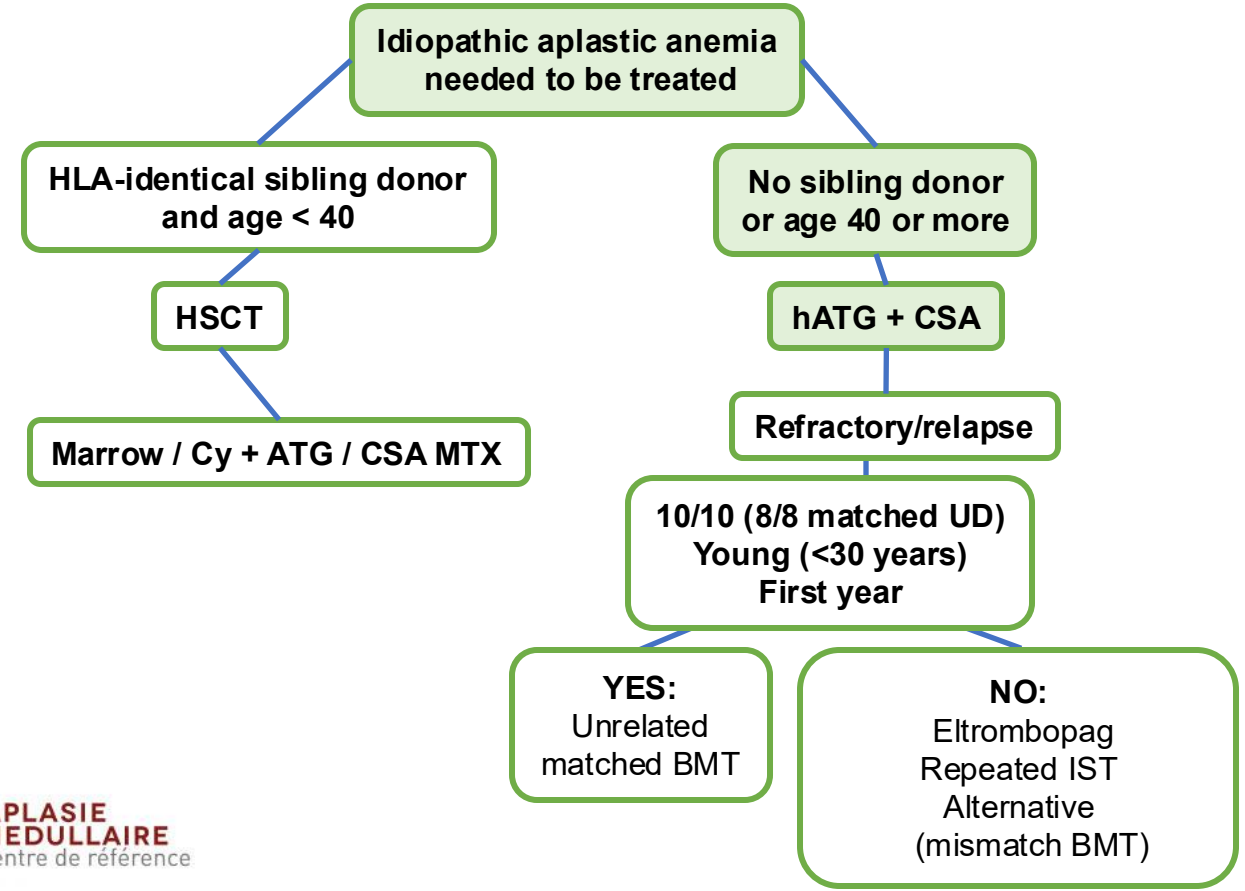
- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

No sibling
No 10/10
Only 9/10 CB or haplo donor

MaRIH

APLASIE MEDULLAIRE centre de référence

Treatment (guidelines)

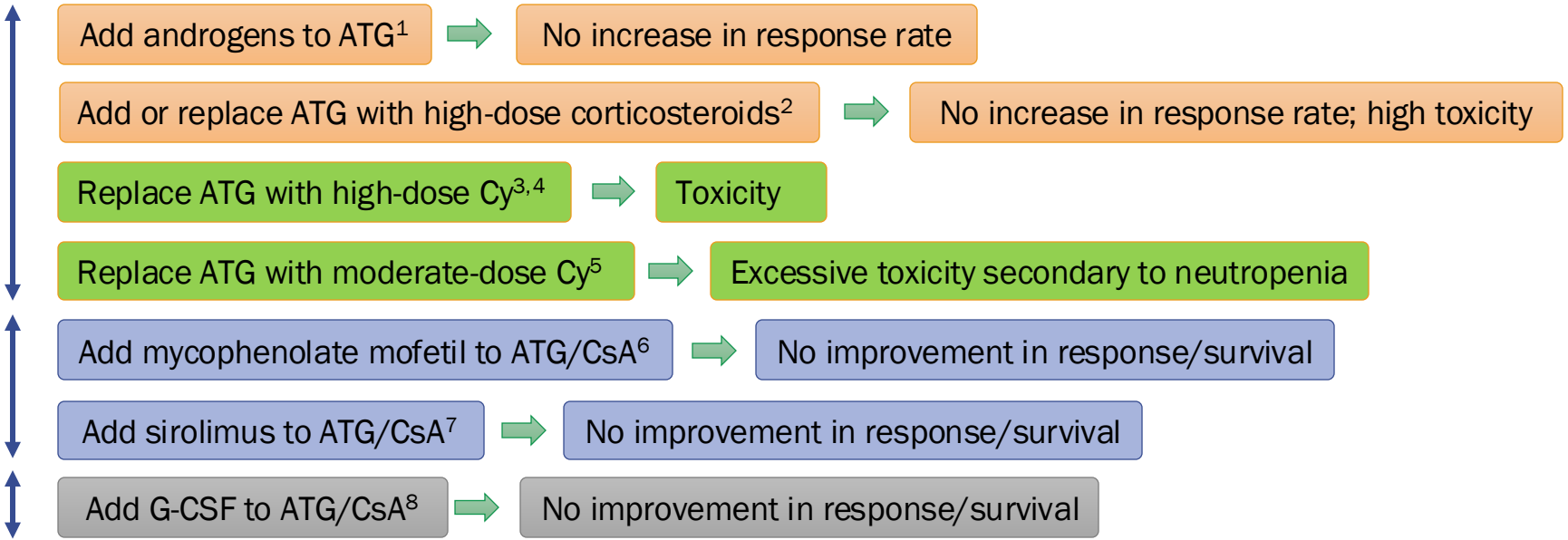


MaRIH

APLASIE MEDULLAIRE centre de référence

How to improve immunosuppression?

- Standard IST for patients with SAA/vSAA who are not eligible for HSCT is **horse antithymocyte globulin (hATG) plus ciclosporin** (CsA) since 30 years

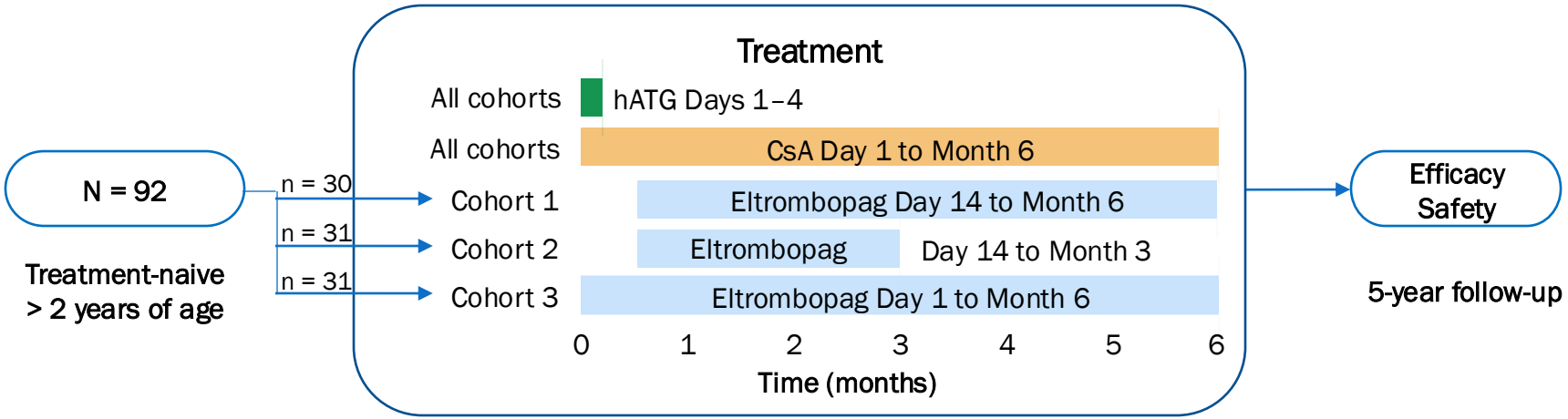


1. Champlin RE, et al. Blood. 1985;66:184-8. 2. Marmont AM, et al. Prog Clin Biol Res. 1984;148:271-87. 3. Tisdale JF, et al. Lancet. 2000;356:1554-9. 4. Tisdale JF, et al. Blood. 2002;100:4668-70. 5. Scheinberg P, et al. Blood. 2014;124:2820-3. 6. Scheinberg P, et al. Br J Haematol. 2006;133:606-11. 7. Scheinberg P, et al. Haematologica. 2009;94:348-54. 8. Locasciulli A, et al. Haematologica. 2004;89:1054-61.

G-CSF, granulocyte-colony stimulating factor.

Eltrombopag first line?

- A phase 2, open-label, interventional, single-arm, sequential cohort study of **eltrombopag in combination with immunosuppression in the first-line** treatment of patients with SAA



Townsley DM, et al. N Engl J Med. 2017;376:1540-50.

Eltrombopag first line?

At 6 months

CR

- Platelet count 100 × 10^9/L
- Neutrophil count ≥ 1 × 10^9/L
- Hemoglobin level 10 g/dL

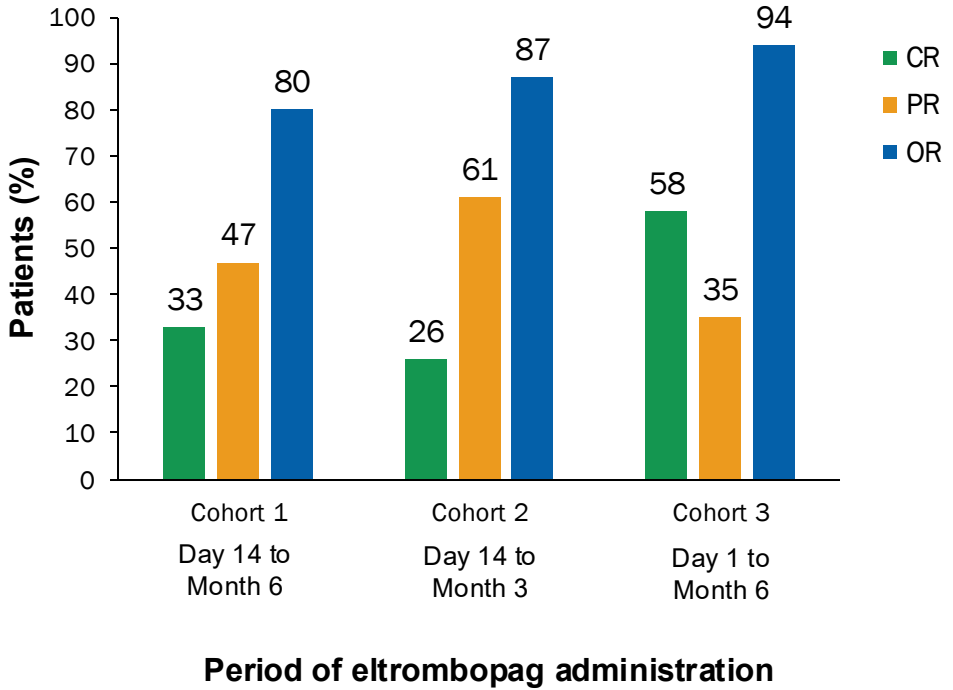
PR

- Blood counts not meeting criteria for SAA or CR

Historical controls IST only

CR 17%

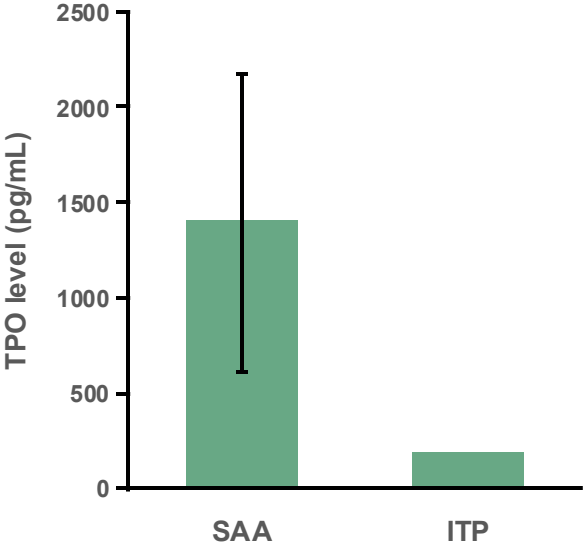
OR 68%



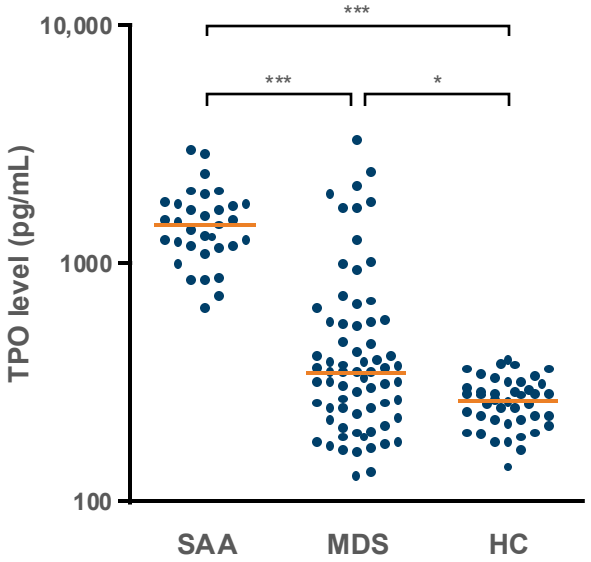
Townsley DM, et al. N Engl J Med. 2017;376:1540-50.

Eltrombopag a surprise? Yes!

Serum TPO levels are markedly elevated in patients with aplastic anemia



Emmons RV *et al. Blood* 1996;87:4068–4071

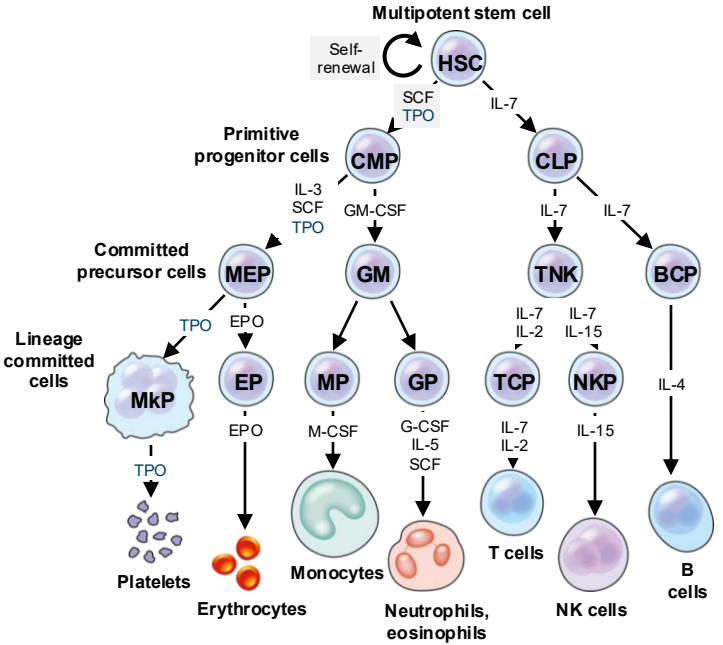


****P*<0.001;**P*<0.05
Feng X *et al. Haematologica* 2011;96:602–606

Eltrombopag a surprise? Possibly not…

- TPO, acting through TPO-R, is essential for normal thrombopoiesis[1]
- TPO-R (c-mpl) is expressed on HSCs[2]
- C-mpl and TPO knock out mice have a reduced number of HSCs
- TPO is able to explend HSCs in vitro[2,3]
- Patients with congenital amegacaryocytosis may eventually evolved to bone marrow failure

TPO: Role in Hematopoiesis



BCP, B-cell progenitor; CLP, common lymphoid progenitor; CMP, common myeloid progenitor; EP, erythroid progenitor; EPO, erythropoietin; GM, granulocyte–macrophage progenitor; GM-CSF, granulocyte-macrophage colony-stimulating factor; GP, granulocyte progenitor; HSC, hematopoietic stem cell; IL, interleukin; MEP, megakaryocyte erythroid progenitor; MkP, megakaryocyte progenitor; MP, monocyte progenitor; NK, natural killer; NKP, natural killer cell progenitor; RBC, red blood cell; SCF, stem cell factor; TCP, T cell progenitor; TNK, T cell natural killer cell progenitor; TPO, thrombopoietin; TPO-R, TPO receptor; WBC, white blood cell. 1. Kaushansky K. *Stem Cells* 1997;15:97–103;
2. Jacobsen SE *et al. Stem Cells* 1996(Suppl 1);173–180; 3. Robb L *et al. Cytokine* 2007;26:6715–6723

Eltrombopag mechanism of action (…)

- The mechanism of action of EPAG in AA **still requires further investigation**.
- Several data have shown that EPAG stimulates hematopoiesis despite high levels of endogenous thrombopoietin (Olnes et al NEJM 2012; Desmond et al Blood 2014). However, it is not clear whether this action is exerted at the **level of hematopoietic stem cells or on more mature progenitor cells** (i.e., increasing the ratio of progenitor/stem cells).
- In addition to its direct stimulatory action on hematopoiesis, EPAG might also contribute to the immunosuppressive effect of ATG and CsA. Indeed, a recent study has shown that EPAG, through its **binding to the transmembrane domain of the thrombopoietin receptor**, prevents the inhibitory effect of IFN-γ by interrupting the interaction between endogenous thrombopoietin and its cognate receptor (i.e., serving as a decoy receptor) (Alvarado LJ et al Blood 2019).
- **Iron chelator**? (Vlachodimitropoulou E et al Blood 2017)

EBMT European Society for Blood and Marrow Transplantation

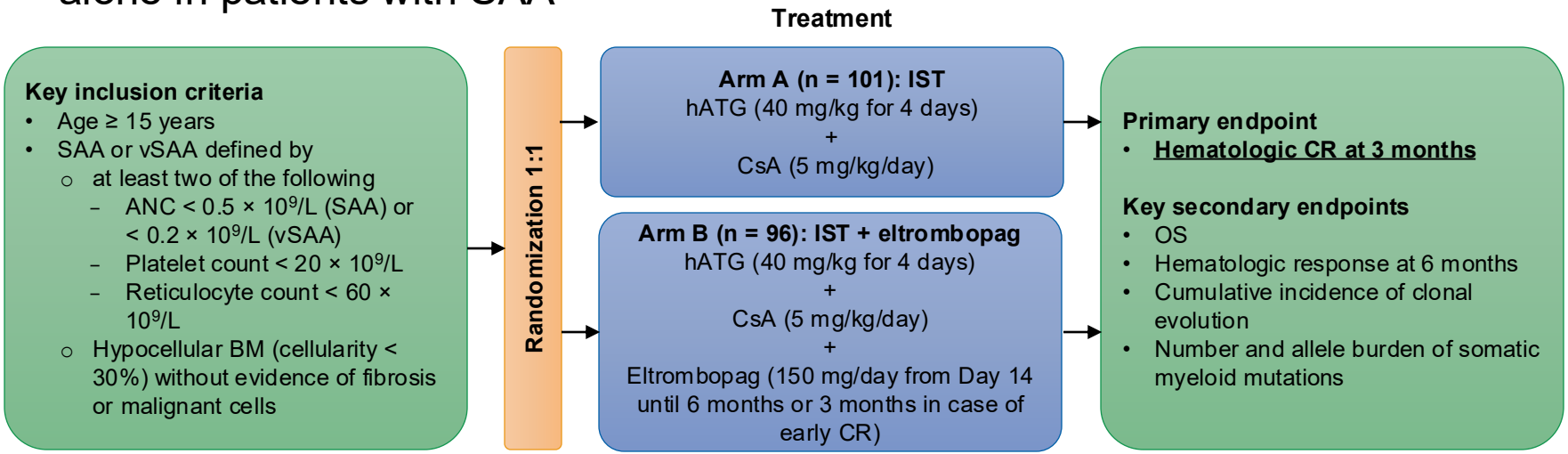
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 6, 2022 VOL. 386 NO. 1

Results of the EBMT SAAWP Phase III Prospective Randomized Multicenter RACE Study of Horse ATG and Ciclosporin with or without Eltrombopag in naïve SAA patients

Régis Peffault de Latour, MD, PhD[1,2*], Judith C.W. Marsh, MD, FRCPath[3], Simona Iacobelli[2,4*], Sofie R. Terwel, MSc[2*], Anita Hill, MD PhD[5*], Constantijn J.M. Halkes, MD[6], Christian Recher, MD, PhD[7], Fiorenza Barraco, MD[8*], Edouard Forcade, MD[9], Juan Carlos Vallejo Llamas[10*], Beatrice Drexler, MD[11*], Jean-Baptiste Mear, MD[12*], Maria Teresa van Lint[13*], Reinier A.P. Raymakers, MD PhD[14*], Marco R De Groot, MD, PhD[15], Etienne Daguindau[16*], Erfan Nur, MD, PhD[17], Wilma Barcellini[18*], Nigel H. Russell, MD[19], Louis Terriou, MD[20*], Anna Paola Iori, MD[21*], Isabel Sánchez- Ortega[22*], Blanca Xicoy, MD, MSc[23*], Isidro Jarque[24*], James Cavenagh[25], Flore Sicre de Fontbrune[1*], Austin Kulasekararaj, MD, MBBS, MRCP, FRCPath[3], Serena Marotta[26*], Talha Munir, MD[5*], Jennifer M.L. Tjon, MD, PhD[6*], Suzanne Tavitian, MD[7*], Aline Praire[8*], Laurence Clement[9*], Florence Rabian, MD[27*], Alexander E Smith, PhD[3*], Riley Cook, MD[3*], Luana Marano[26*], Morag Griffin, MD[5*], Elena Palmisani[28*], Petra Muus, MD, PhD[3], Fabiana Cacace[26*], Jakob R. Passweg, MD, MS[11], Gerard Socie, MD, PhD[1], Ghulam J. Mufti, MBBS, FRCP, FRCPath, DM[3*], Carlo Dufour[2,28] and Antonio M. Risitano, MD, PhD[2,26]

Race design

- The **RACE trial** is an investigator-driven, open-label, phase 3, randomized trial comparing the combination of hATG, CsA, and eltrombopag with IST alone in patients with SAA



Central laboratory King's college, London

Stratification based on **disease severity, age** and **center**

ANC, absolute neuthrophil count; vSAA, very severe aplastic anemia.

RACE definitions & study design

- **RACE criteria for response**
  - **CR:** Hb >100 g/L, neutrophils >1.0x109/L and platelets >100x109/L
  - **PR:** no longer meets SAA criteria, **Transfusion independence**, Hb >8gr/dL, neutrophils >0.5x109/L and platelets >20x109/L
  - **NR**: not meeting criteria for response
- **Clonal evolution**
  - Acute leukemia, myelodysplastic syndrome and/or new karyotypic abnormality
- **Primary endpoint**
  - To detect an increase in CR from 7% in arm A to 21% in arm B at 3m (at least 96 patients per arm)

NIH study versus RACE

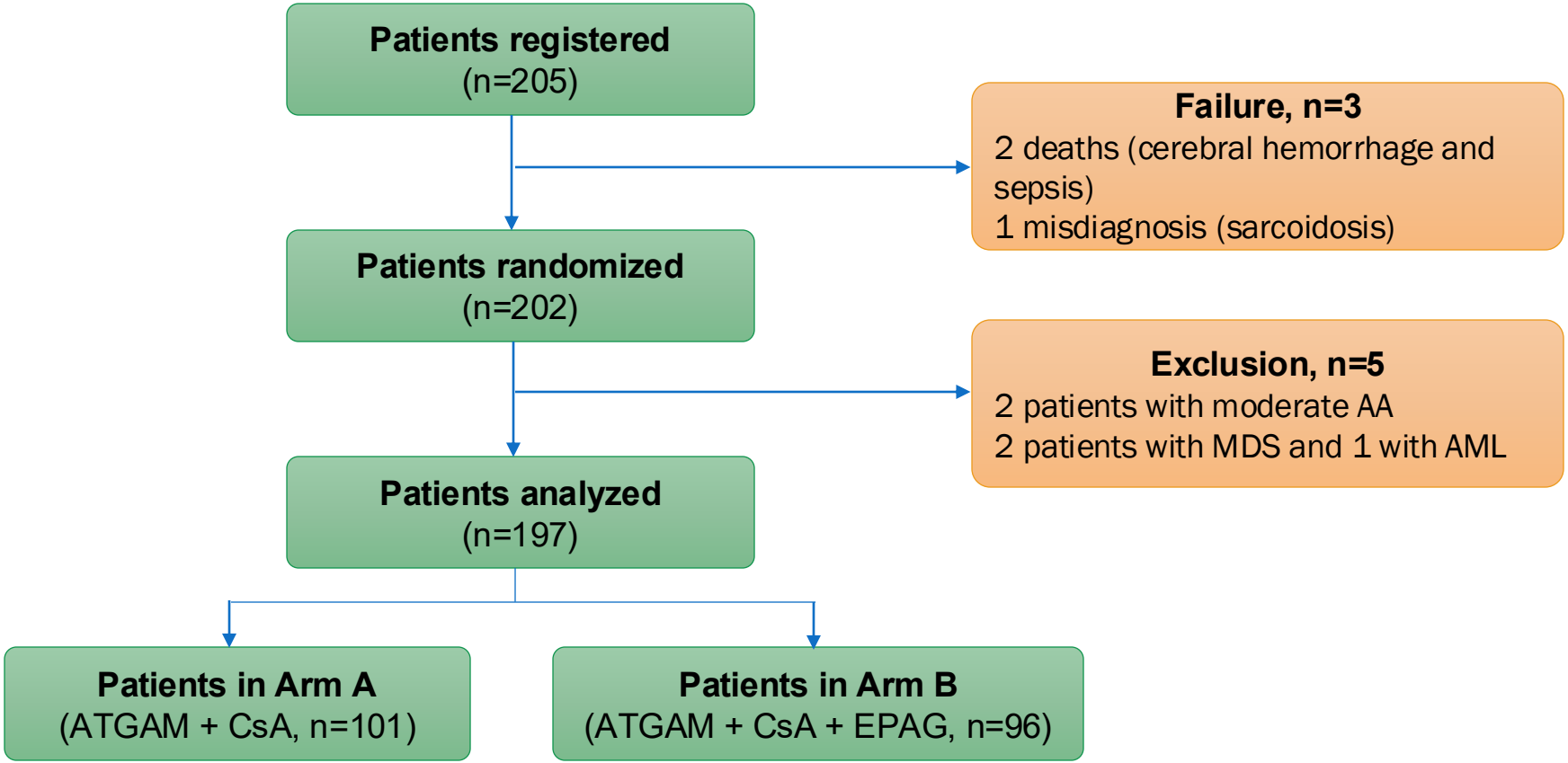
	NIH study[1]	RACE[2]
Study design	Non-randomized, historically controlled	Randomized, controlled
CsA treatment duration	6 months + low dose for up to 24 months	1 year + low dose for up to 24 months
Eltrombopag initiation	On Day 1 in Cohort 3 On Day 14 in Cohort 1 and 2	On Day 14
Eltrombopag treatment duration	6 months in Cohort 1 and 3 3 months in Cohort 2	6 months 3 months with early CR
Primary endpoint	CR and PR at 6 months	CR at 3 months
Criteria for response	PR: transfusion independency not needed	PR: transfusion independency required
Minimum age of inclusion, years	2	15
Median age of patients, years	32	53

1. Townsley DM, et al. N Engl J Med. 2017;376:1540-50.
2. Peffault de Latour R, et al., unpublished data. Accepted for oral presentation at EBMT 2020; abstract GS2-2.

RACE trial

- **Inclusion period**: July 2015 - April 2019
- **Patients**: 205 treatment naïve patients enrolled in 6 countries and 24 sites
- **Median Follow-up: 24** months

RACE flow chart



Baseline characteristics

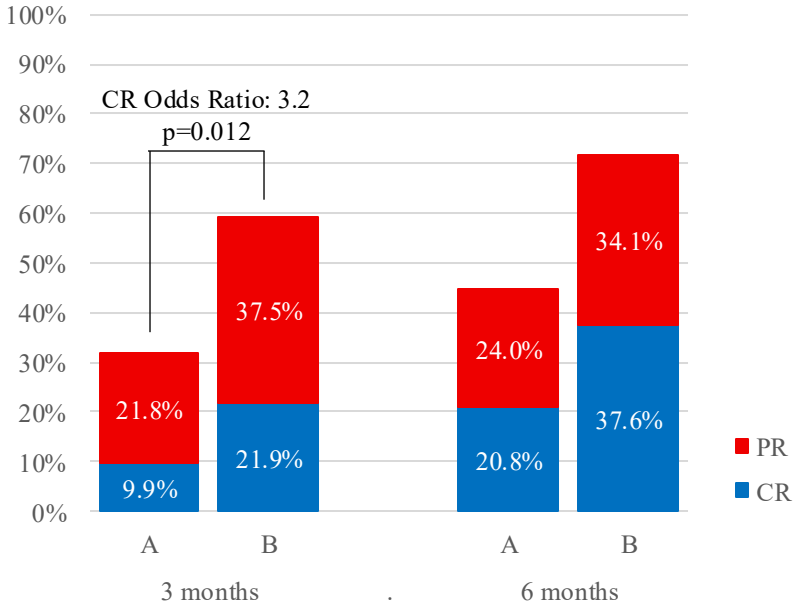
	Arm A	Arm B	Total
No. of patients	101 (51.3%)	96 (48.7%)	197 (100%)
Age (median, min-max)	52 (15-81)	55 (16-77)	53 (15-81)
Age categories (n, %)			
<18 y	7 (6.9%)	2 (2.1%)	9 (4.6%)
18-<40	29 (28.7%)	27 (28.1%)	56 (28.4%)
40-<65	43 (42.6%)	43 (44.8%)	86 (43.7%)
>65	22 (21.8)	24 (25.0%)	46 (23.4%)
Sex (n, %)			
Male	52 (51.5%)	56 (58.3%)	108 (54.8%)
Female	49 (48.5%)	40 (41.7%)	89 (45.2%)
Severity of AA (n, %)			
SAA	67 (66.3%)	62 (64.6%)	129 (65.5%)
vSAA	34 (33.7%)	34 (35.4%)	68 (34.5%)
PNH granulocytes >1.0% (n, %)	44 (44.9%)	33 (35.5%)	77 (40.3%)

Hematological response

- The **RACE study** was powered to detect an increase in CR from 7% in arm A to 21% in arm B at 3 months (primary endpoint).

- **CR at 3 months*:**
  - Arm A: 9.9% & Arm B: 21.9%
  - Pooled Odds Ratio 3.2, p=0.012

- **OR at 6 months (preliminary analysis n=181)*:**
  - Arm A: 44.8% & Arm B: 71.8%
  - Pooled Odds Ratio: 3.7



*Prior transplantation, clonal evolution or death were considered as no response at 3 and 6m

Hematological response (NIH criteria)

NIH criteria = PR: transfusion independency not needed

		Response at 3 months			Response at 6 months		
		hATG + CsA (Arm A)	**hATG + CsA + EPAG (Arm B)**	**OR (95%CI)* (p-value)**	**hATG + CsA (Arm A)**	**hATG + CsA + EPAG (Arm B)**	**OR (95%CI)* (p-value)**
	CR	10 (9.9%)	21 (21.9%)	**3.2 (1.3-7.8) (p=0.012)**	20 (19.8%)	30 (31.6%)	**2.3 (1.1-4.7) (p=0.019)**
	PR	55 (54.5%)	51 (53.1%)		47 (46.5%)	44 (46.3%)	
	No response	33 (32.7%)	22 (22.9%)		34 (33.7%)	20 (21.1%)	
	Unclassified	3 (3.0%)	2 (2.1%)		0 (0.0%)	1 (1.0%)	
	CR+PR (OR)	65 (66.3%)	72 (76.6%)	**2.2 (1.1-4.4) (p=0.033)**	67 (66.3%)	74 (78.7%)	**2.2 (1.1-4.3) (p=0.026)**

Cohort 2 NIH (EPAG day 14 > 3 months): CR 26%, PR 61%, OR 87% at 6 months

Safety

	Arm A	Arm B	Total
Serious Adverse Events*	135	145	280
Fatal cases	14	8	22
Patients coming off study treatment prematurely requiring second line HSCT	13	11	24
Pregnancy	3	1	4

**Events are classified per SOC (system organ class) according to the CTCAE (Common Terminology Criteria for Adverse Events (US National Cancer Institute of the National Institutes of Health).*

Clonal evolution – myeloid malignancy

Arm	Age	AA	Cytogenetics/Karyotypic abnormalities			CE	MDS	somatic mutations +VAF			Response		Relapse
			Baseline	6 months	24 months			Baseline	6 months	24 months	3 mo	6 mo	
A	58	SAA	46XY	46, XY, +Y, -7[4]/46, XY[11]		Yes-6 mo	No	BCOR 0.1%, DNMT3A 1.24%, TET2 0.1%	BCOR 5.01%, DNMT3A 13.24% TET2 13.29%	NST	PR	CE	Yes
B	19	SAA	46,XX[16]	Not done or failed (del13q at 12 &18 months)	Normal	Yes-12 mo	Yes	PIGA 7.74%	PIGA 7.15%	NST	PR	CR	No
B	62	SAA	46,XY [15]	46,XY,-13(q13q34)[2]/46,XY[18]	Unknown (persistent del13q at 12 and 18 months)	Yes-6 mo	No	No mutations	No mutations	NST	NR	NR	No
A	67	SAA	46, XY [20]	45,X,-Y[3]/46,XY[17]	46,XY,del(7)(q22q3?2)[7] /46,XY[18] (No del7q detected 6 and 12 months later)	No	No	No mutations	No mutations	BCOR 1.97%	NR	NR	No

Clonal evolution – somatic mutations

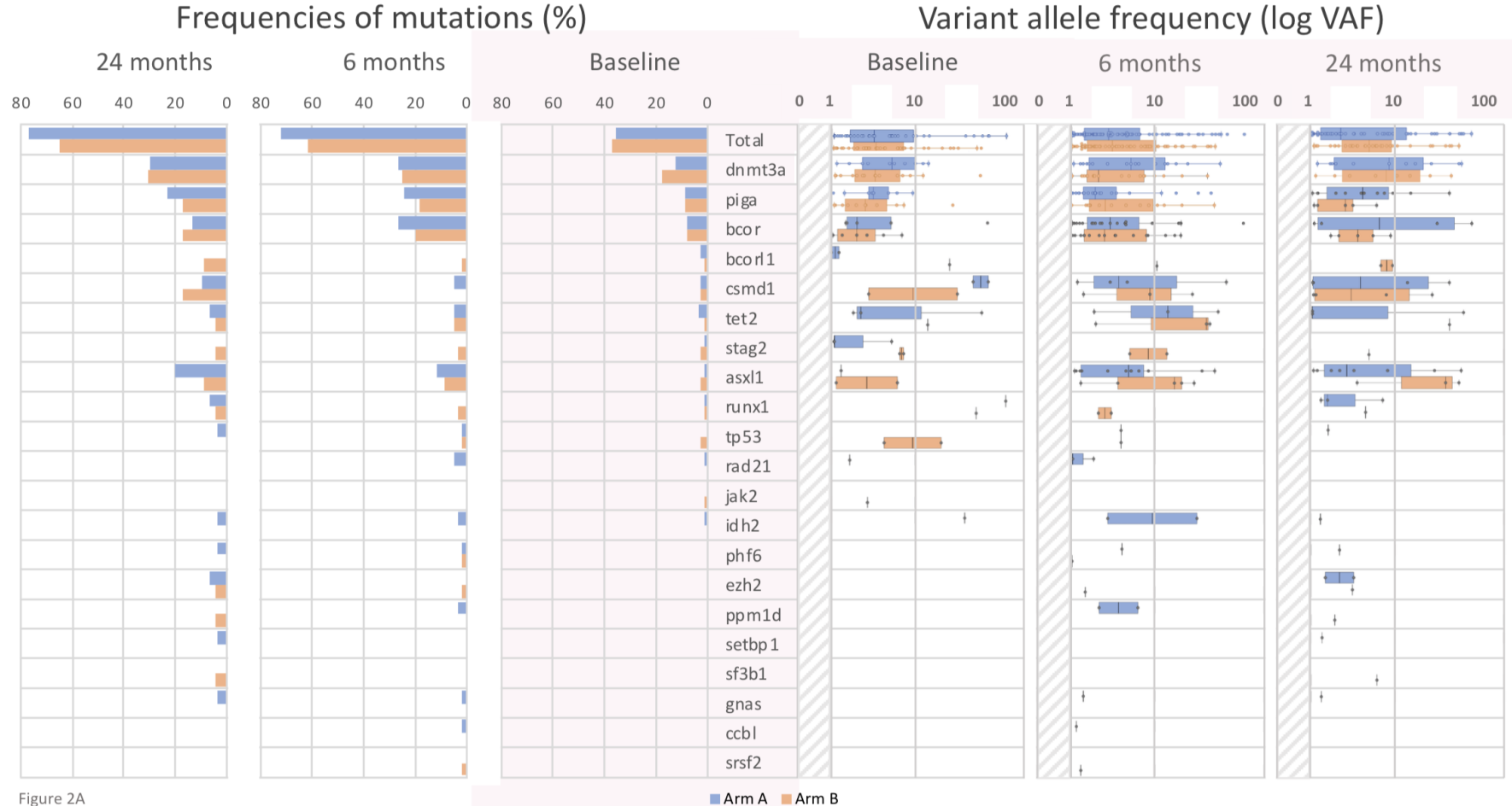


Figure 2A

Fatal cases

Cause of death	Arm A	Arm B	Total
Hemorrhages	2	0	2
Infections	9	4	13
Salvage treatment	1	0	1
Others:	2	4	6
• Acute Respiratory Distress Syndrome	0	1	1
• Aortic valve disease	0	1	1
• Concomitant lung cancer	1	0	1
• Encephalopathy of unknown origin	1	0	1
• Tamponade	0	1	1
• Thrombosis	0	1	1
Total	***14***	***8***	***22***

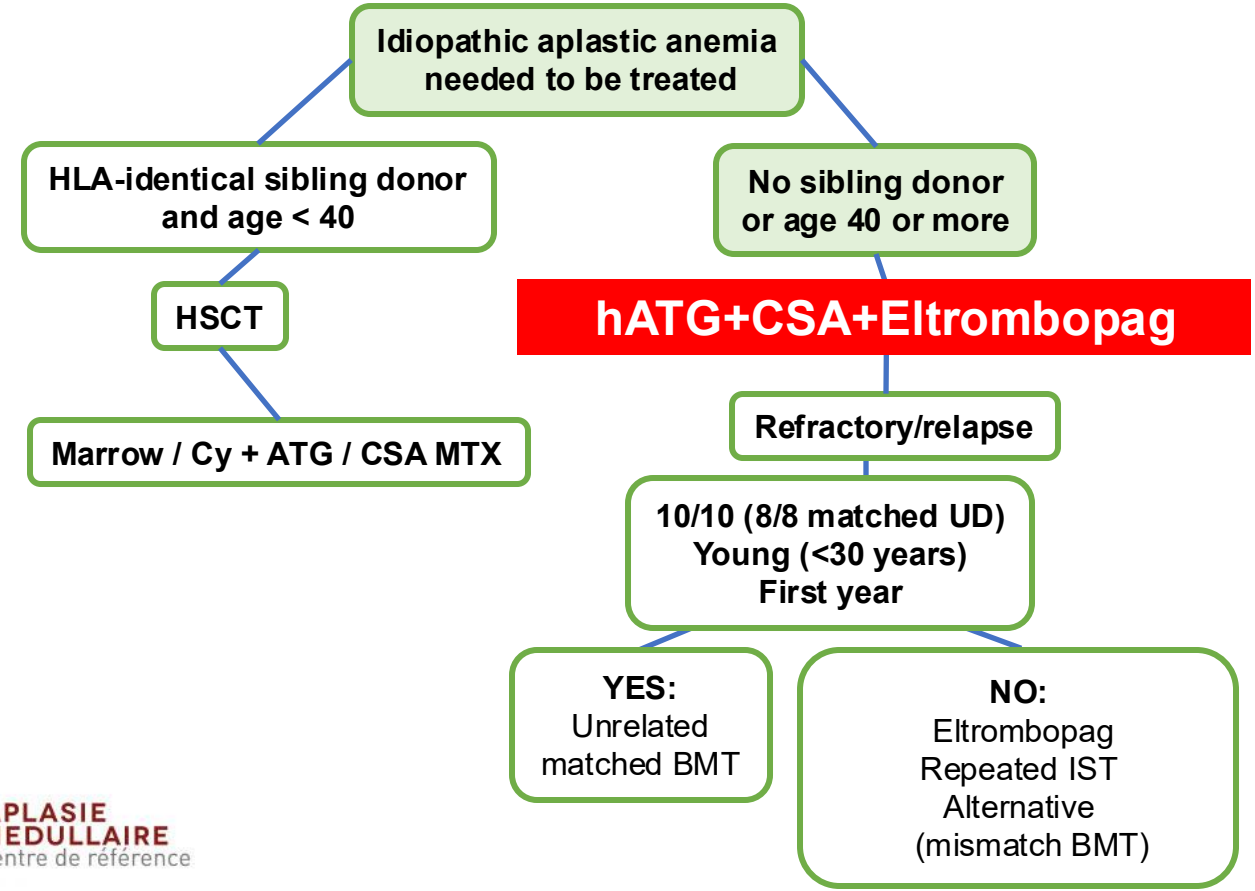
Conclusion - Perspectives

- EPAG, when added to standard IST (hATG and CsA), **significantly increases the rate of CR at 3 months** in untreated patients with SAA with **no safety concern** at time of analysis (18 months median follow-up).

- **Somatic myeloid mutations assessment (on going):** high sensitivity next generation sequencing analysis was performed at baseline, 6 months and 24 months using a 31 gene target molecular bar coded panel central analysis (central analysis at King's College, London).

- Clonal evolution occurs 10-15 years after the diagnosis of aplastic anemia; the **Long term follow-up study (RACE-2)** is being set-up to answer this question in the future

Treatment (guidelines)



MaRIH

APLASIE MEDULLAIRE centre de référence

Patient case

- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

Refractory at 6 months …

MaRIH

APLASIE MEDULLAIRE centre de référence

Patient case

- Male, 17 years old
- Aplastic anemia:
  - Hb: 4.8 g/dL; Neutrophils: 0.75 x 10^9/L; Platelets: 11 x 10^9/L; Reticulocytes: 35 x 10^9/L)
  - Cytogenetics showed a normal male karyotype
  - **Hypocellular bone marrow (<5%) with no dysplasia**
- Acquired:
  - Normal CBCs 10 years before
  - No family history
  - Normal physical exam
  - PNH positive (3%) – FA & Telomeropathy negative

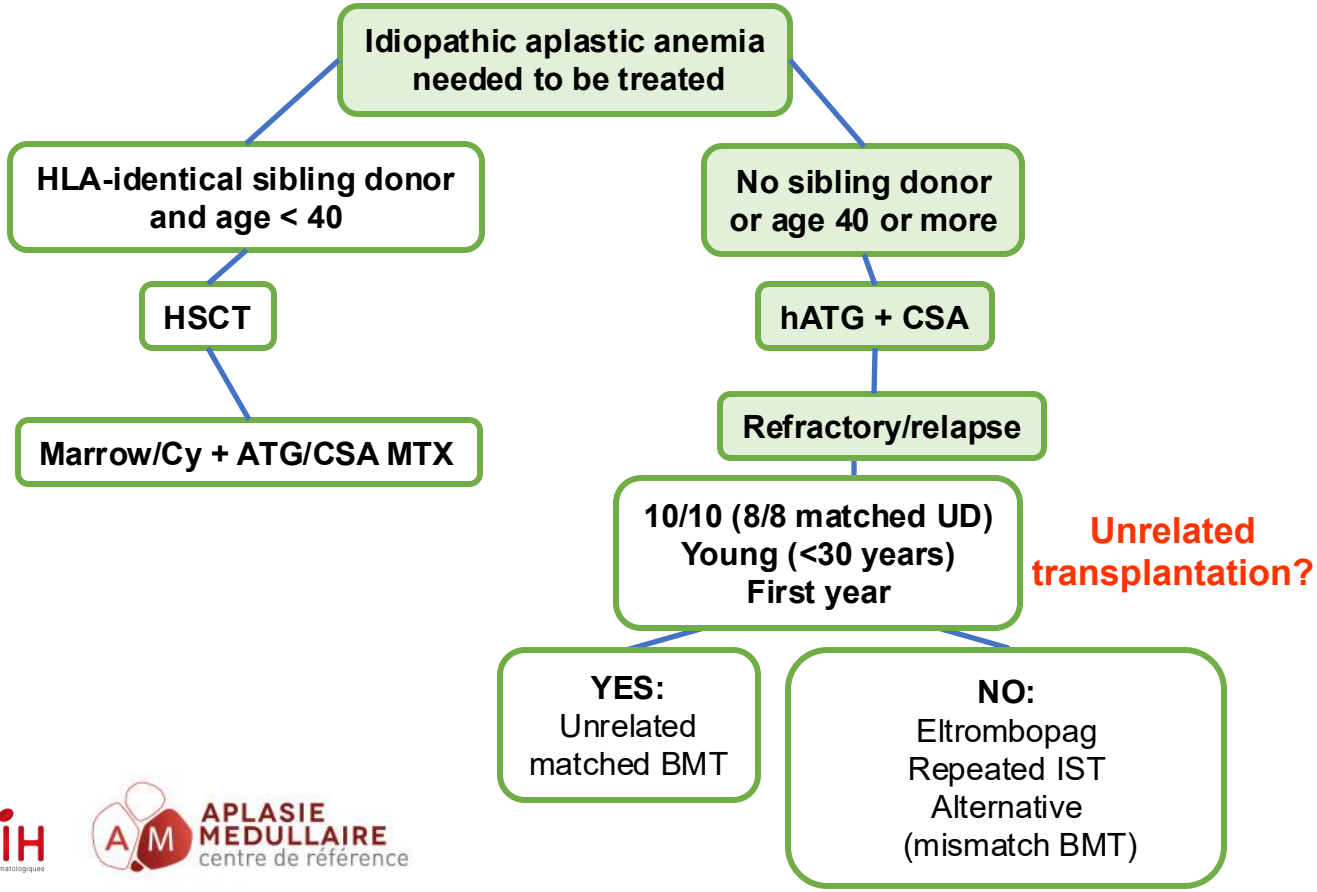
Refractory at 6 months …

Inherited disorders? Clonal evolution?

MaRIH

APLASIE MEDULLAIRE centre de référence

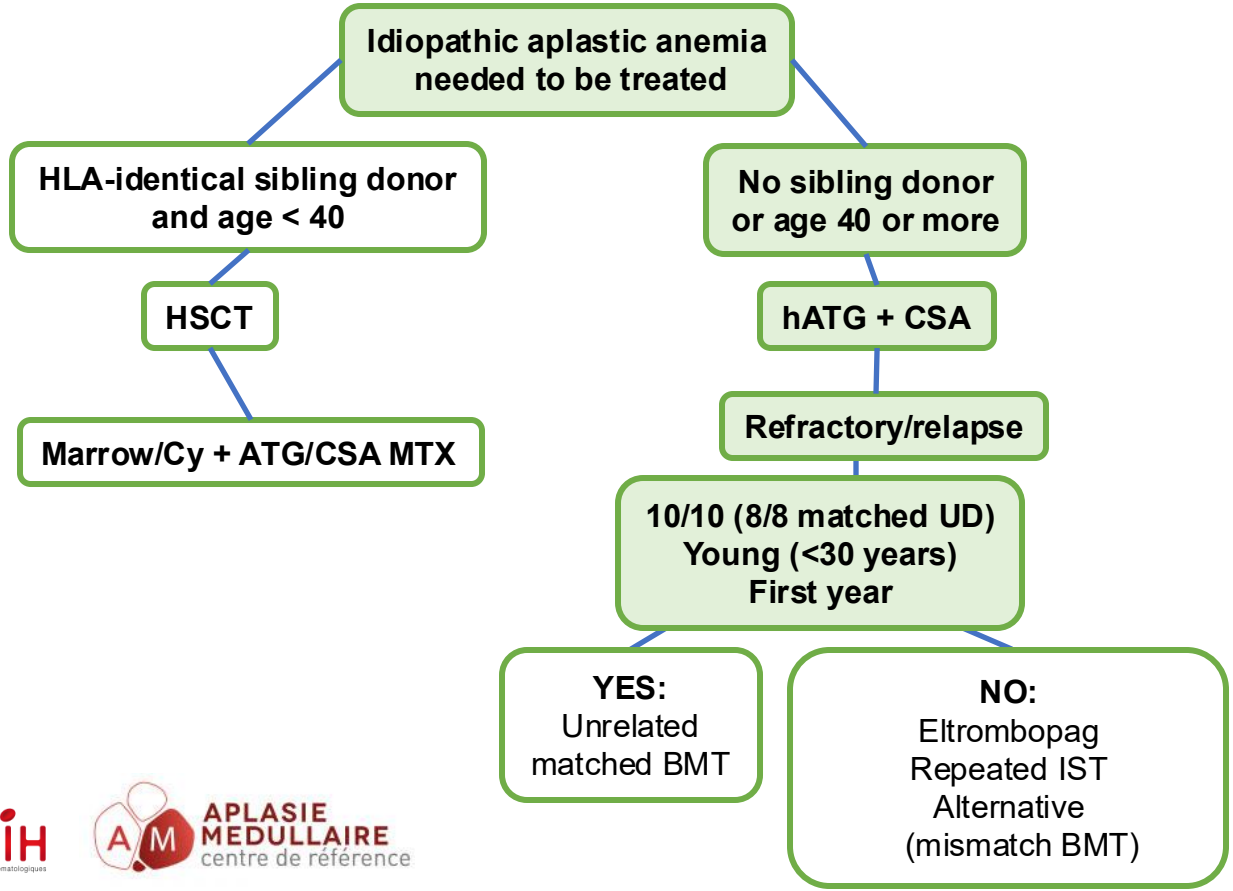
Treatment (guidelines)



MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

APLASIE MEDULLAIRE
centre de référence

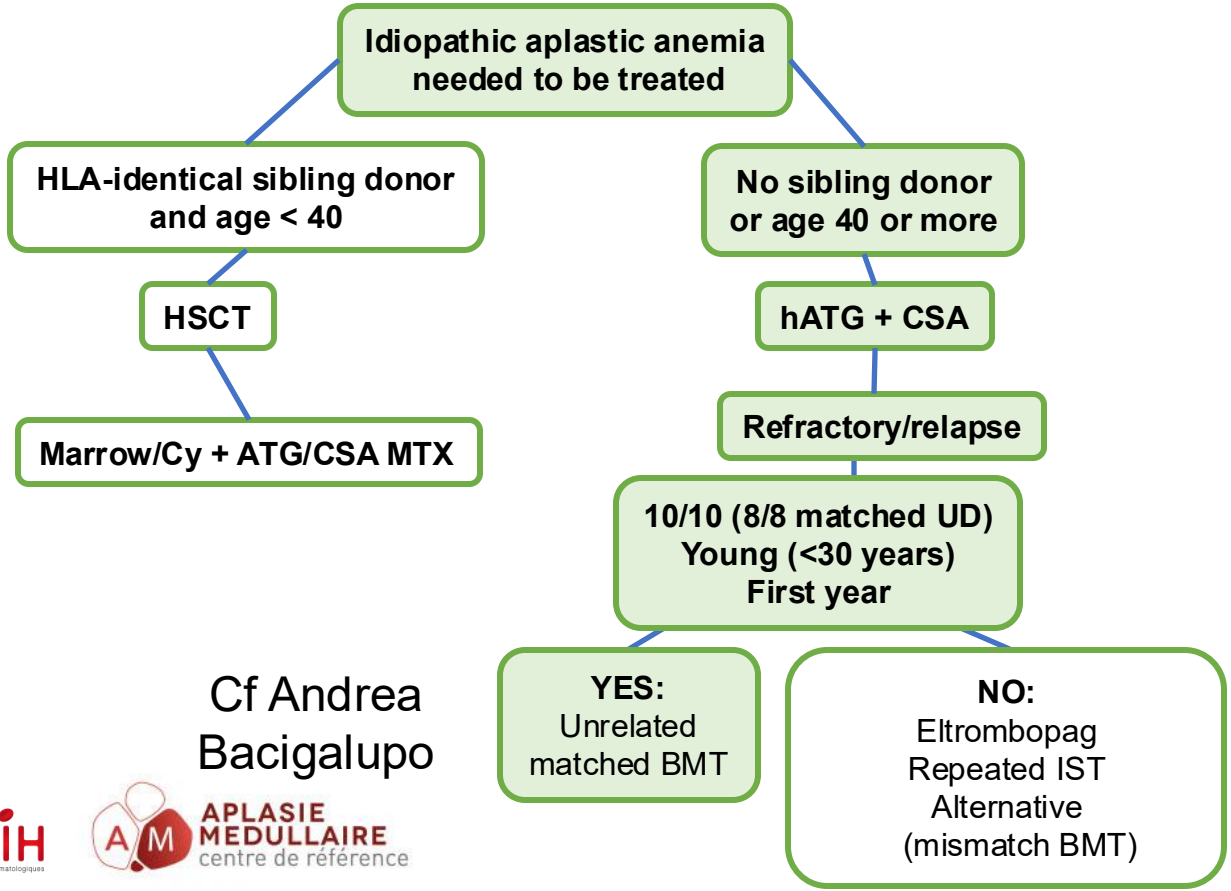
Treatment (guidelines)



MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

APLASIE MEDULLAIRE
centre de référence

Treatment (guidelines)

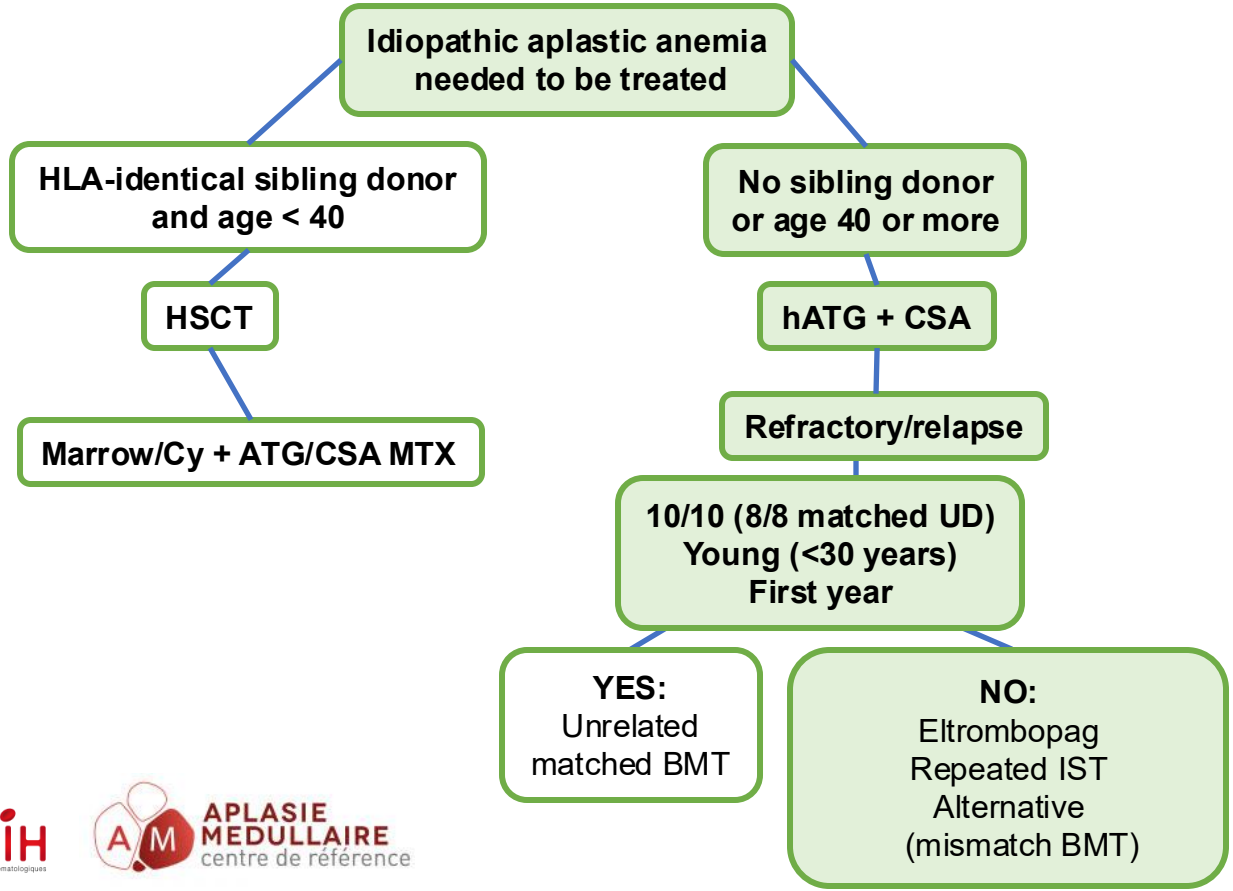


Cf Andrea Bacigalupo

MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

APLASIE MEDULLAIRE
centre de référence

Treatment (guidelines)

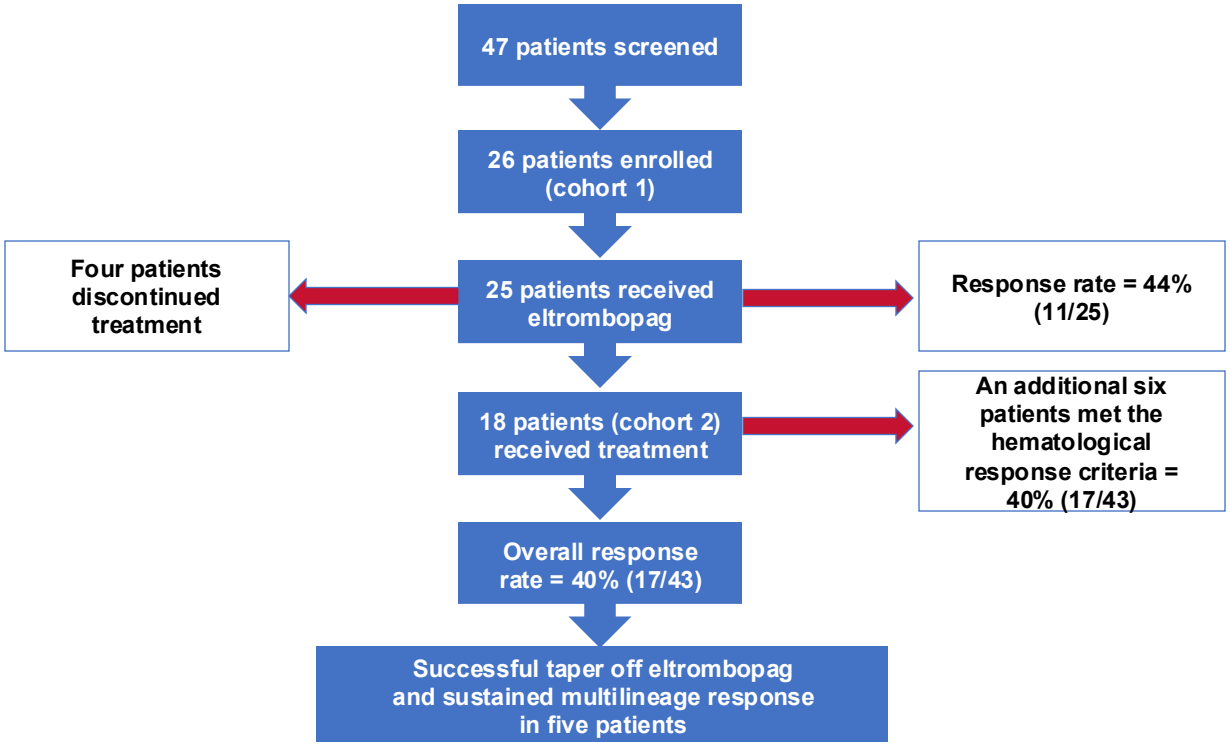


MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

APLASIE MEDULLAIRE
centre de référence

TPO receptor agonist and refractory aplastic anemia

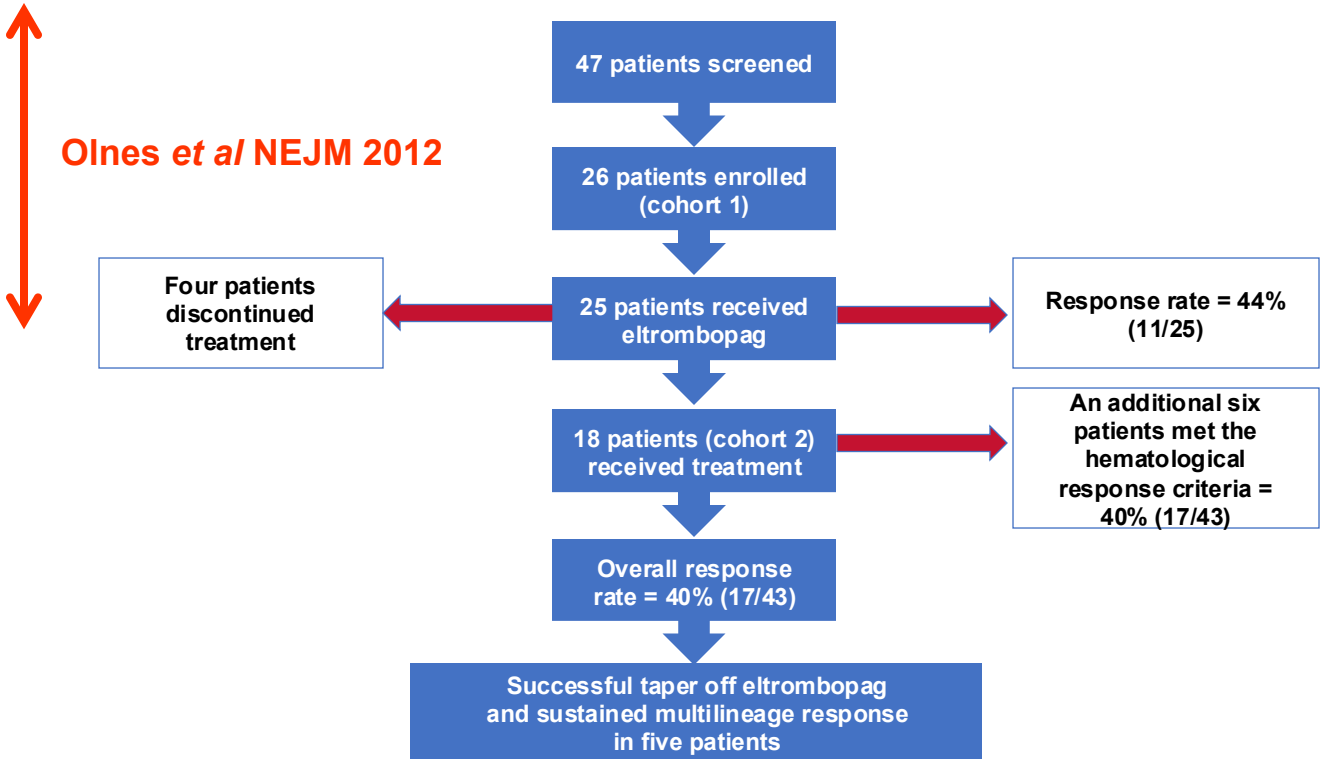
Response rate



Adapted from Olnes M, *et al.* N Engl J Med. 2012;367:11-9. Desmond R, *et al.* Blood. 2014;123:1818-25.

TPO receptor agonist and refractory aplastic anemia

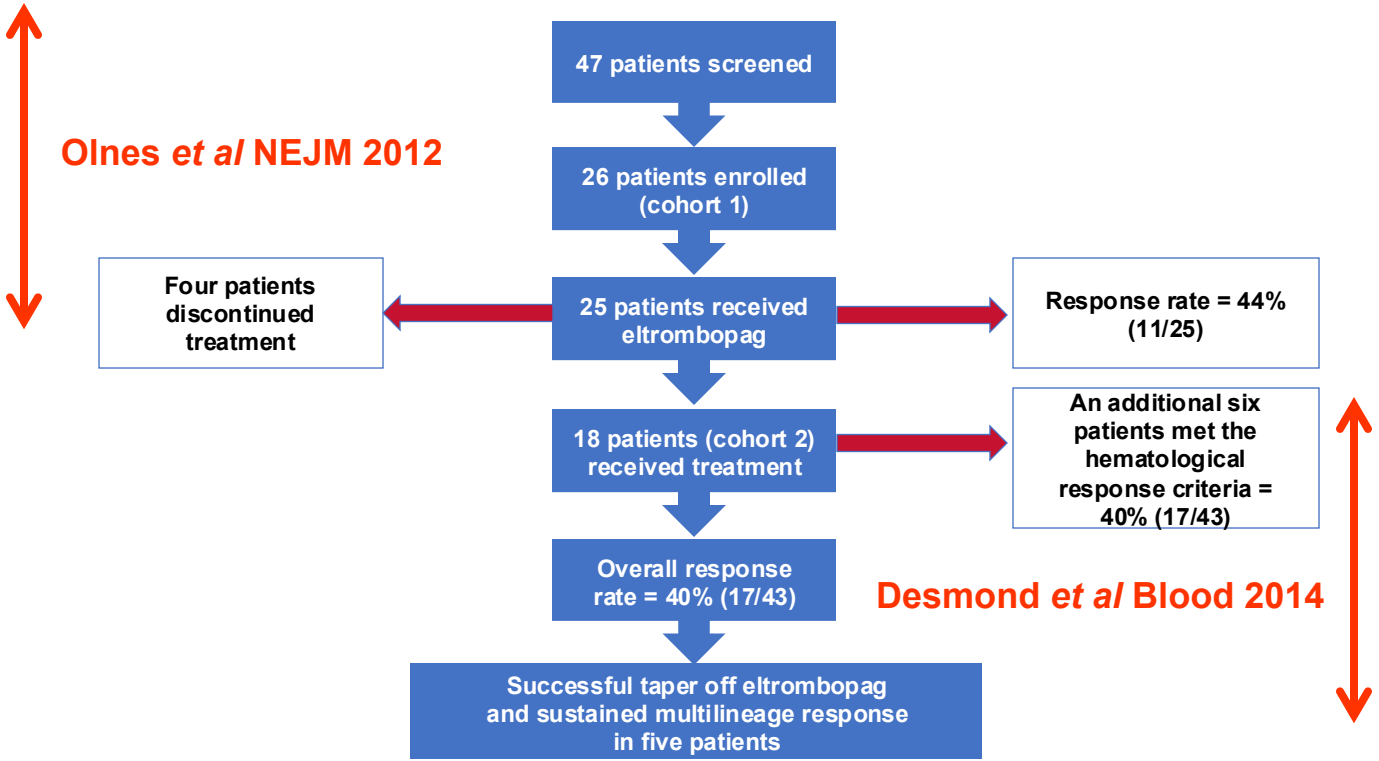
Response rate



Adapted from Olnes M, *et al.* N Engl J Med. 2012;367:11-9. Desmond R, *et al.* Blood. 2014;123:1818-25.

TPO receptor agonist and refractory aplastic anemia

Response rate

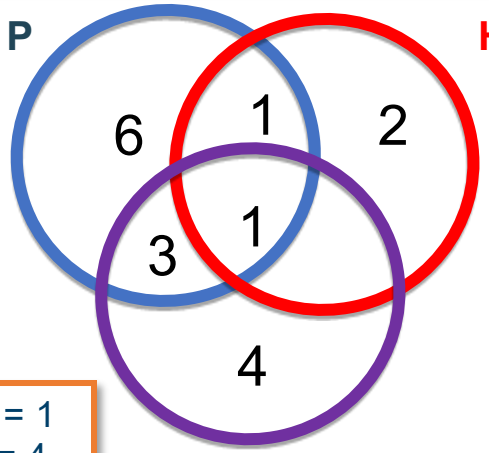


Adapted from Olnes M, *et al.* N Engl J Med. 2012;367:11-9. Desmond R, *et al.* Blood. 2014;123:1818-25.

Phase II study of eltrombopag in refractory AA

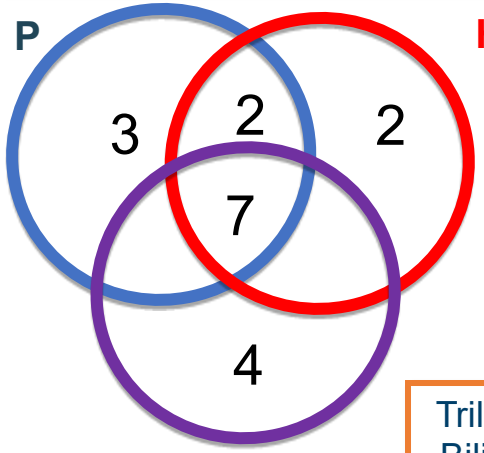
Mutlilineage responses

16 Weeks – primary endpoint



Trilineage = 1
Bilineage = 4
Unilinege = 12

Best response at follow-up



Trilineage = 7
Bilineage = 2
Unilinege = 9

Platelets
Hemoglobin
Neutrophils

Durable multilineage responses are possible after treatment with eltrombopag in refractory AA
Patients can become red blood cell and platelet transfusion independent

AA, aplastic anemia.
Desmond R, *et al.* Blood. 2014;123:1818-25.

TPO receptor agonist and refractory aplastic anemia

French experience - patients characteristics

- ATG-naïve patients (Cohort A, n=11)
- Refractory patients (Cohort B, n=35)

- Disease characteristics:

	Cohort A	Cohort B	p-value
no. (%) [IQR]	**11**	**35**	
Demographic characteristics			
Age at diagnosis (y)	73.7 [60.9, 77.5]	53.4 [26.3, 67.3]	0.003
Age at ELT initiation (y)	74.1 [67.4, 78.0]	55.3 [35.9, 68.5]	0.003
Male (%)	4 (36.4)	21 (60.0)	0.298
Aplastic anemia characteristics			0.152
Idiopathic, no PHN clone	4 (36.4)	23 (65.7)	
Idiopathic, with PHN clone	6 (54.5)	11 (31.4)	
Dyskeratosis congenita	1 (9.1)	1 (2.9)	

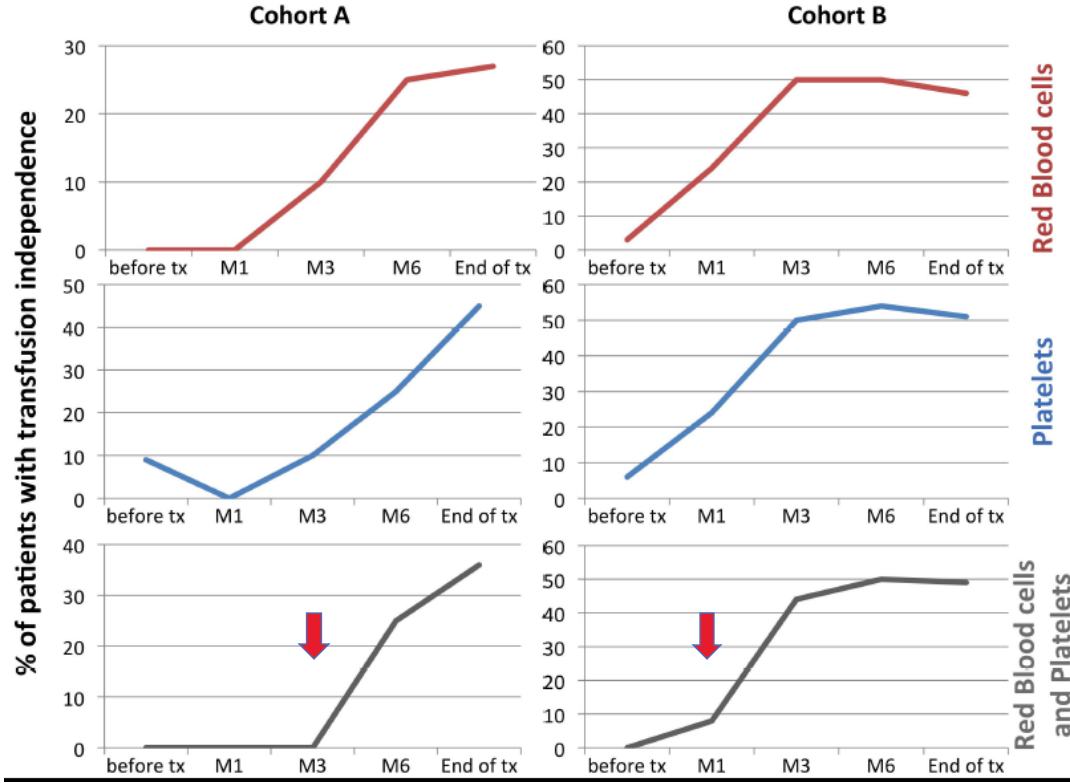
APLASIE MEDULLAIRE centre de référence

Lengliné et al, Haematologica 2017

MaRIH

TPO receptor agonist and refractory aplastic anemia

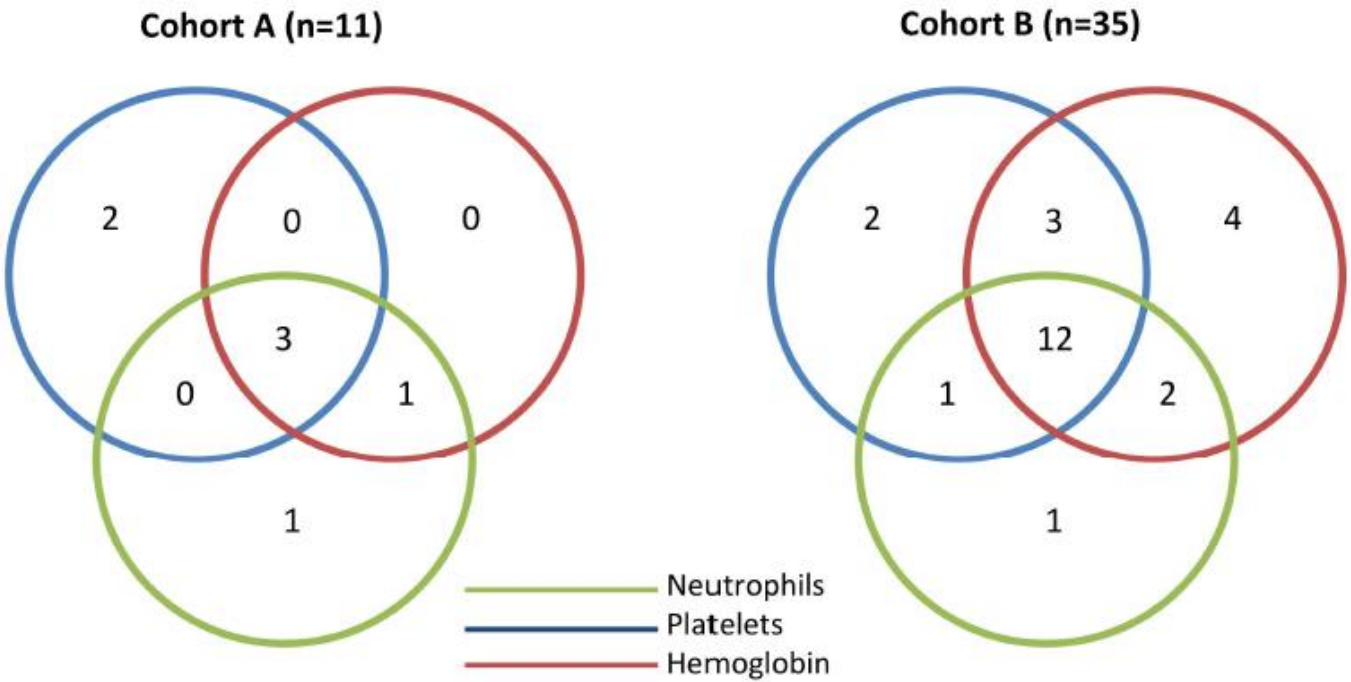
French experience – response rates



Lengliné et al, Haematologica In press

TPO receptor agonist and refractory aplastic anemia

French experience - type of response



Durable multilineage responses are possible after treatment with eltrombopag in refractory AA
Patients can become red blood cell and platelet transfusion independent

Lengliné et al, Haematologica In press

TPO receptor agonist and refractory aplastic anemia

French experience - main messages

- **Safety**
  - 1 SAE (liver toxicity)
  - Clonal evolution (lack of follow-up …)
- **Response rate = 40%**
  - 3 months for refractory patients; 6 months for 1st line
  - Multi-lineage response = 30% among responders
- **Of note**
  - 20% of non responders responded at a higher dose (225 mg*)
  - Possible drug discontinuation (if robust response)
  - Second IST including ATG (Revolade-ATG-CSA) lead to excellent results in refractory patients (response rate = 100% but n=8)

APLASIE MEDULLAIRE centre de référence

Lengliné *et al,* Haematologica 2017

MaRIH

TPO receptor agonist and refractory aplastic anemia

Treatment stop

Robust responders*

- Platelets >50×10^9/L
- Hb >10 g/dL
- Neutrophils >1×10^9/L
- **>8 weeks**

↓

Decrease dose by 50%

↓

Counts remain above limits for **8 weeks**

↓

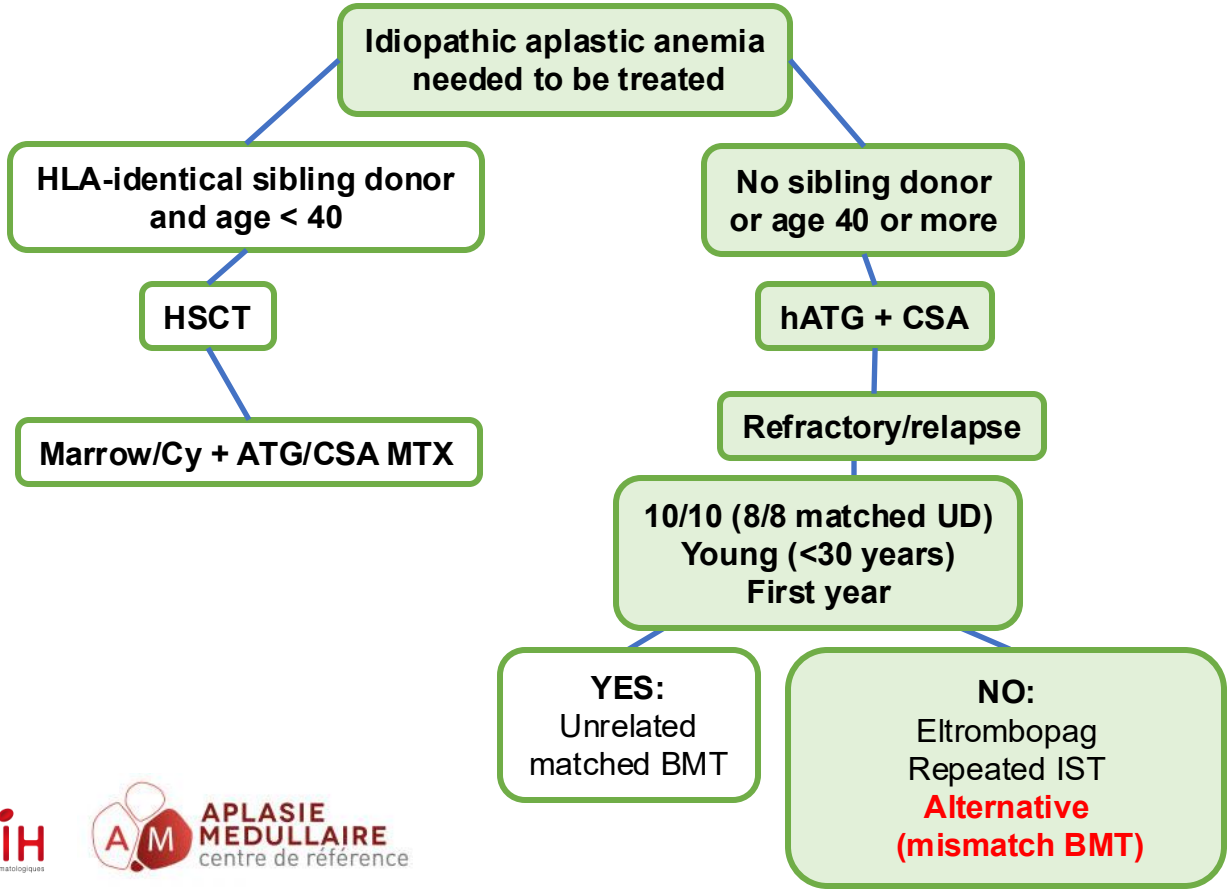
Discontinue drug

*De[illegible]ond R *et al. Blood* 2014;123:1818–1825;

- **15** Patients stopped for ELT failure
- **1** Patients stopped for toxicity
- **4** Patients were able to taper and discontinue ELT treatment if they met the trilineage hematopoiesis criteria for >8 weeks
  - Four patients (n=46) fulfilled these criteria
  - All had eltrombopag tapered successfully to off drug
  - All remain in remission after a follow-up off drug of 7, 12, 24 and 27 months

Lengliné et al, Haematologica In press

Treatment (guidelines)



Cf Andrea Bacigalupo

MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

AM APLASIE MEDULLAIRE centre de référence

Conclusion

- **First line treatment:**
  - MRD = choice treatment 1st line for patients of 40 years old or less
  - MUD 1st line is still experimental (only pediatric)
  - hATG+CSA+Eltrombopag for the others

- **Refractory patients:**
  - MUD for patients with refractory AA of 30 years old or less is standard of care
  - Alternative BMT mainly for young patients (20 year or less)
  - Eltrombopag for the others (if no already used first line)

Thank you!

The French Reference Center for aplastic anemia and PNH in Paris

Saint-Louis Hospital

Robert Debré Hospital

Institute of Hematology, IUH St-Louis

F Sicre, T Leblanc, JH Dalle, A Baruchel, G Socié,
N Vasquez, W. Cuccuini, J Soulier (Fanconi team),
C Kannengiesser, E Lainey, L Da Costa (Telomeres team)

APLASIE MEDULLAIRE centre de référence

MaRIH
Filière de santé Maladies Rares ImmunoHématologiques

SFGM TC
Société Francophone de GREFFE DE MOELLE et de Thérapie Cellulaire

2016 EBMT
European Society for Blood and Marrow Transplantation