RACCOLTA E TRAPIANTO DI CELLULE STAMINALI EMOPOIETICHE

TRAPIANTO DI CELLULE STAMINALI EMOPOIETICHE

E' la trasfusione di cellule staminali emopoietiche prelevate in quantita' adeguata da un donatore idoneo (*trapianto allogenico*) o dal paziente stesso (*trapianto autologo*)

HEMATOPOIETIC STEM CELL TRANSPLANTATION

TYPE OF TRANSPLANT	*DONOR*	*HLA MATCHING*	*SOURCE OF HSC*
SYNGENIC	SIBLING	IDENTICAL	BM or PB
ALLOGENIC	SIBLING UNRELATED	IDENTICAL IDENTICAL or MISMATCHED	BM, PB, CB
	SIBLING PARENT CHILD	MISMATCHED	
AUTOLOGOUS	SELF		BM or PB

FREQUENZA DELLE CELLULE STAMINALI CD34

- *MIDOLLO OSSEO:*
  - CONDIZIONI BASALI 1%
  - STIMOLATO 5%
- *SANGUE PERIFERICO*
  - CONDIZIONI BASALI 0.1%
  - STIMOLATO 1%

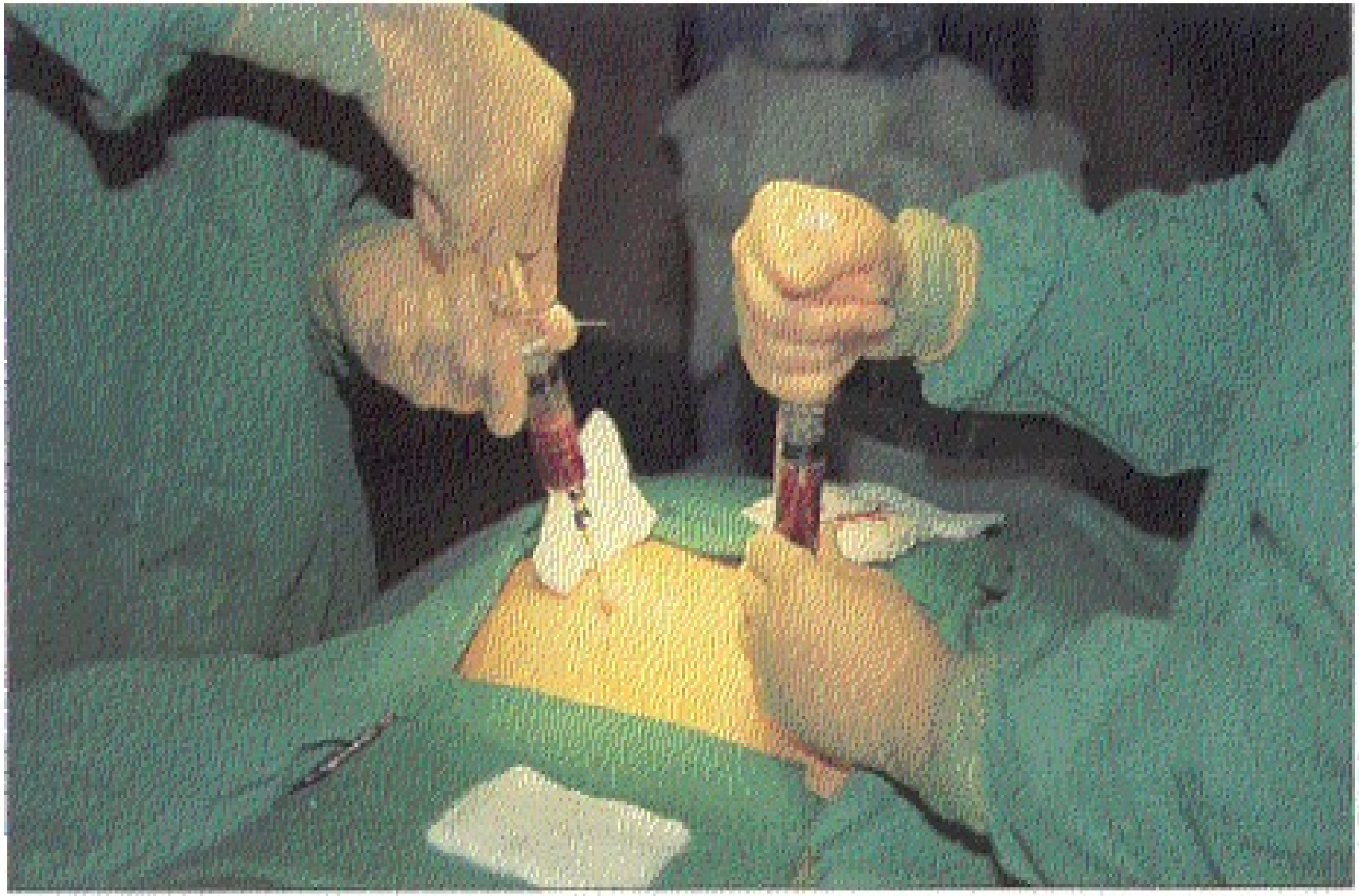
RACCOLTA CELLULE STAMINALI
MIDOLLO

ASPIRAZIONI MULTIPLE DALLA CRESTA ILIACA POSTERIORE IN ANESTESIA GENERALE.

(cresta iliaca anteriore e sterno)

IL MIDOLLO VIENE ASPIRATO, PROCESSATO E QUINDI CRIOPRESERVATO O SUBITO REINFUSO

RACCOLTA DI CELLULE STAMINALI DA MIDOLLO OSSEO

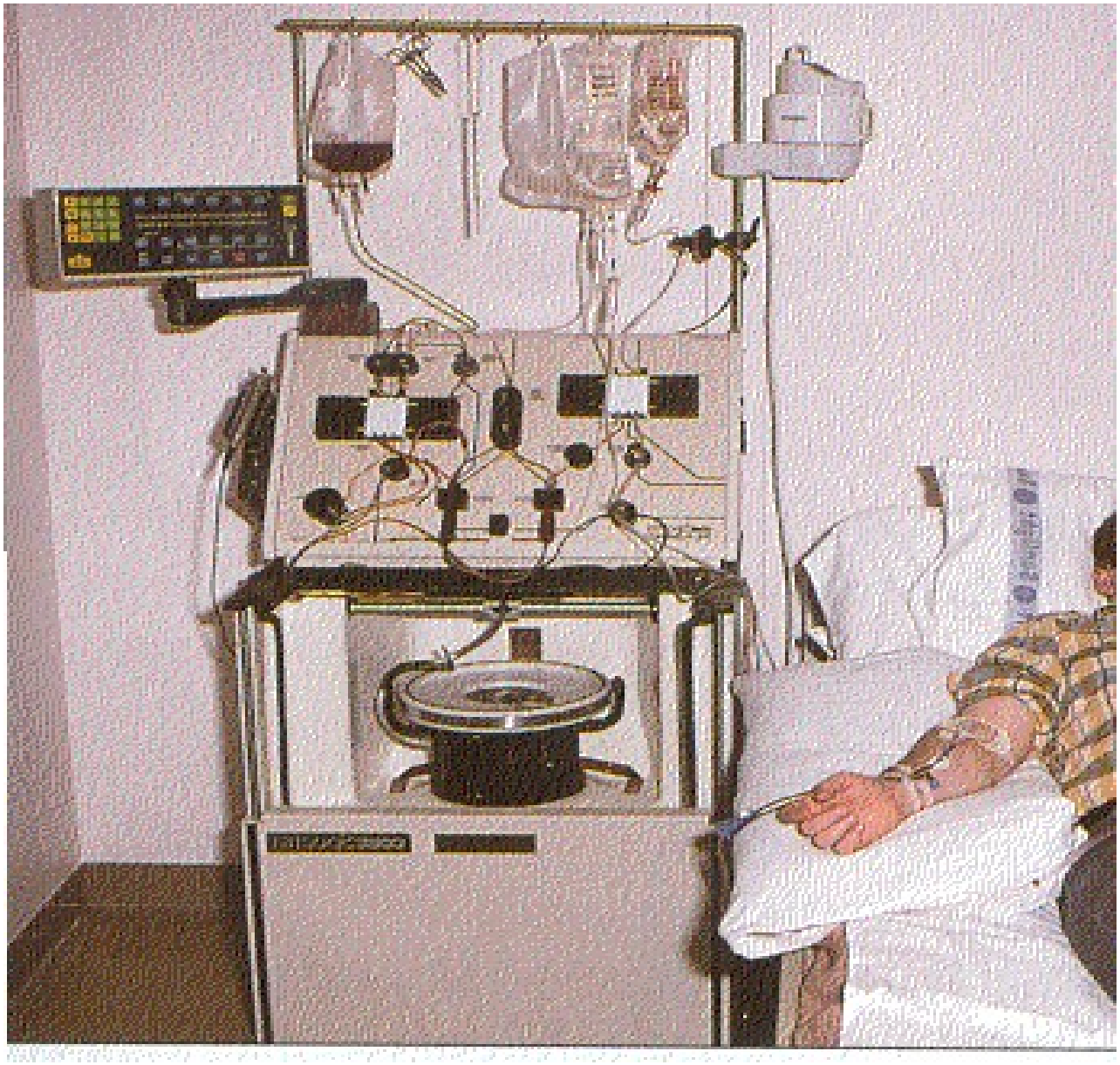


RACCOLTA CELLULE STAMINALI
SANGUE PERIFERICO

- La raccolta di cellule staminali da sangue periferico avviene tramite passaggio del sangue in una macchina che e' in grado di identificare le cellule staminali e di trattenerle, restituendo tutte le altre cellule al paziente.

- Le cellule staminali cosi' raccolte vengono concentrate e criopreservate o subito reinfuse.

RACCOLTA DI CELLULE STAMINALI DA SANGUE PERIFERICO



Criopreservazione delle cellule staminali emopoietiche (CSE)

- CSE vitali per 2-3 giorni a temperature > a t. di congelamento
- La criopreservazione mantiene inalterate le caratteristiche biologiche oltre i limiti di tempo naturali.
- Si esegue con congelatore programmato in azoto liquido

- **Possibili danni della crioconservazione**:

1. Cristalli di ghiaccio e danno degli organuli cellulari
2. Cristalli di ghiaccio extracellulari e disidratazione delle cellule
3. Reidratazione ed espansione delle cellule durante lo scongelamento
4. Funzionamento parziale degli enzimi cellulari a basse temperature con possibile accumulo di metaboliti tossici intermedi

Criopreservazione delle cellule staminali emopoietiche (CSE)

Crioconservante:
dimetilsulfossido (DMSO) al 5-10%
(disidratazione parziale intracellulare)

Principi base:

- **DMSO aggiunto al plasma pochi ml alla volta mentre viene raffreddato su ghiaccio (reazione esotermica) → midollo**
- **Viene mantenuto lo stesso profilo termico delle componenti della miscela**
- **Controllo della velocità di raffreddamento**

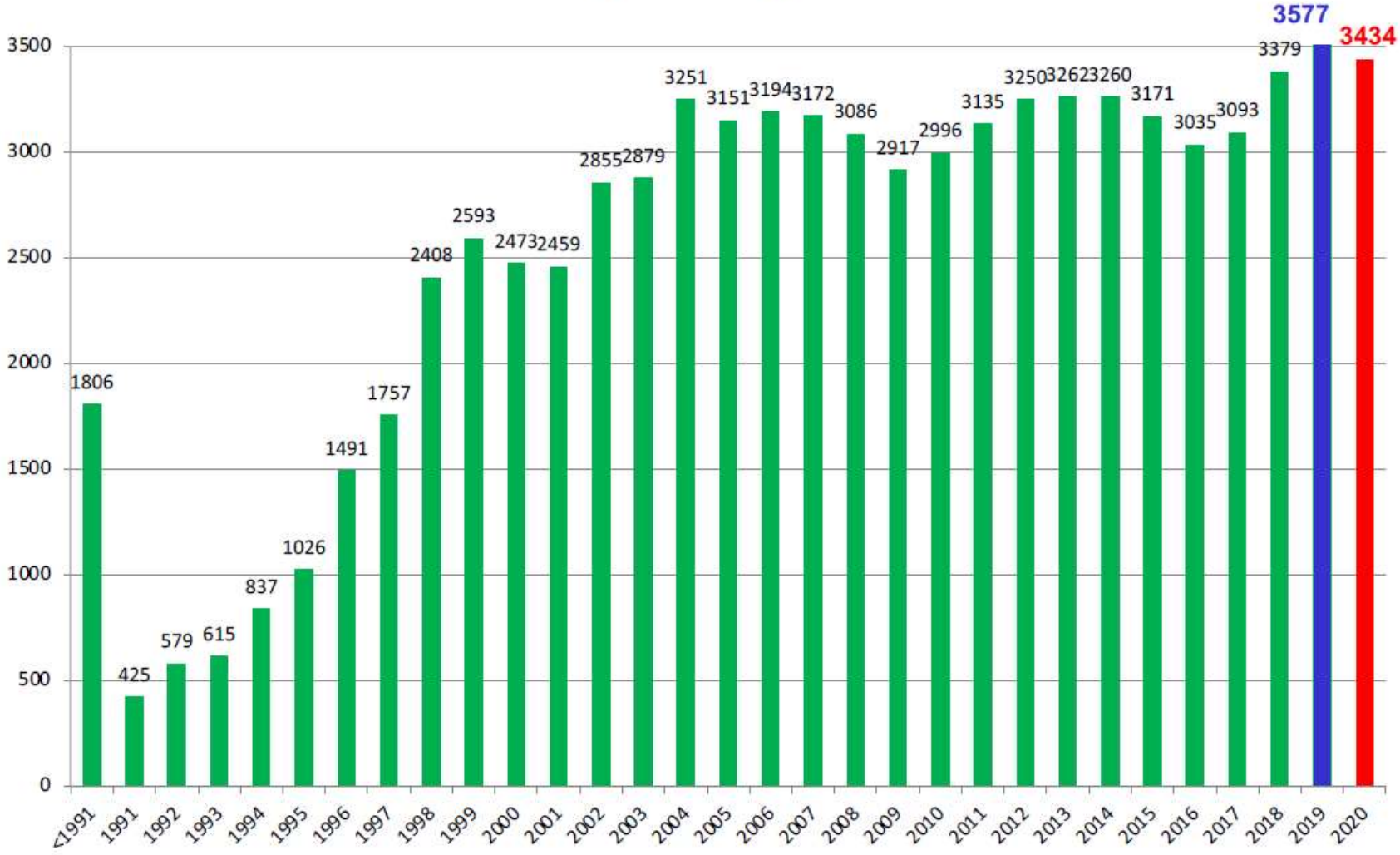
Crioconservazione e scongelamento

- A lungo termine a -196 °C, a -80°C per brevi periodi
- Tempo 3-5 anni (max 10 anni ma con controllo della vitalità)
- Scongelamento delle sacche a bagno maria (37-38°C) nel più breve tempo possibile
- Reinfusione subito dopo lo scongelamento

Trapianto di cellule staminali emopoietiche autologhe

- Condizionamento: intensificazione della chemioterapia ovvero chemioterapia ad alte dosi
- Reinfusione delle CSE autologhe: funzione di “salvataggio”
- Efficacia terapeutica dal regime di condizionamento NON dalla reinfusione delle CSE autologhe

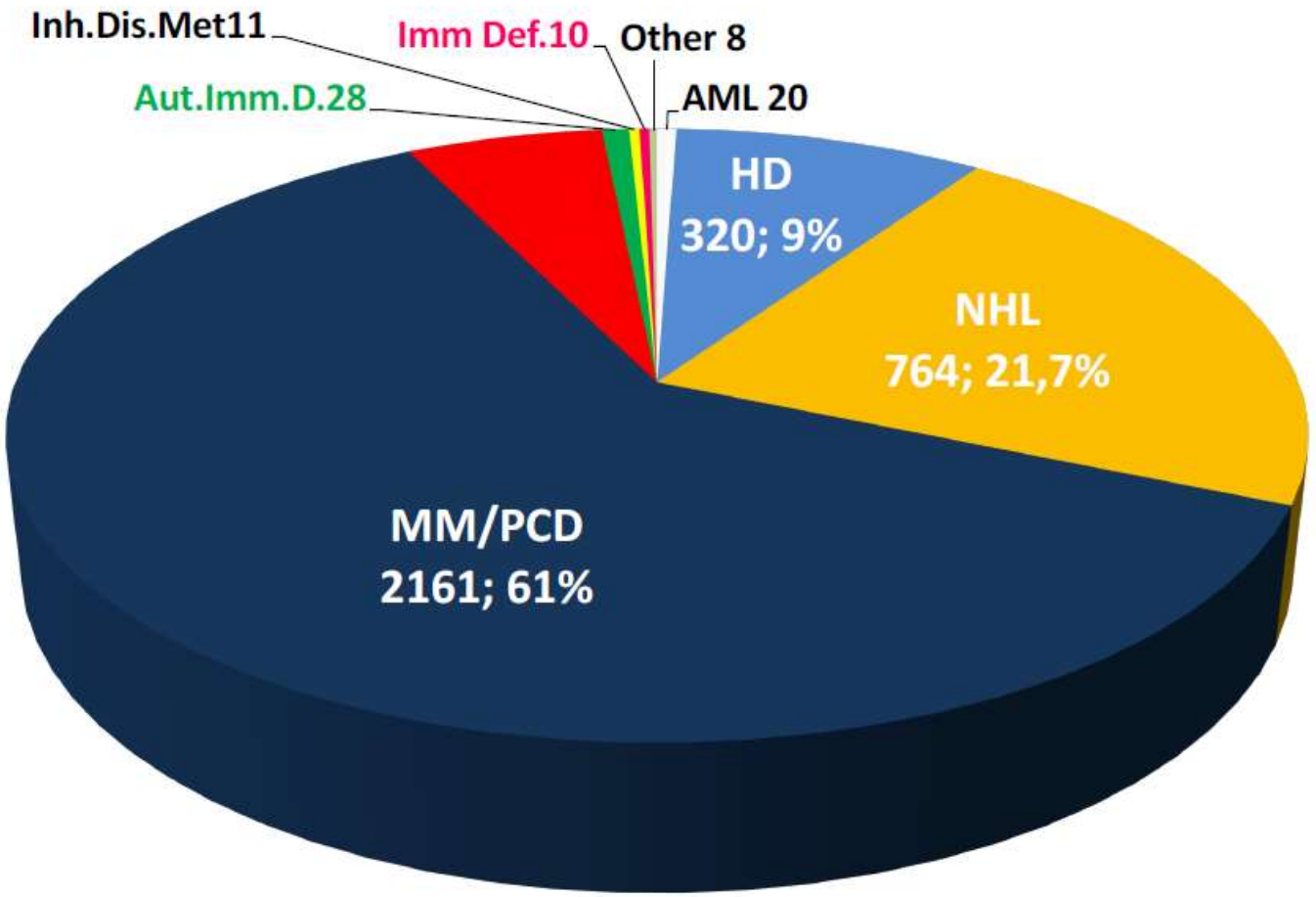
Autologous Transplants
(n=78.566)



Export date 06/03/2021

GITMO

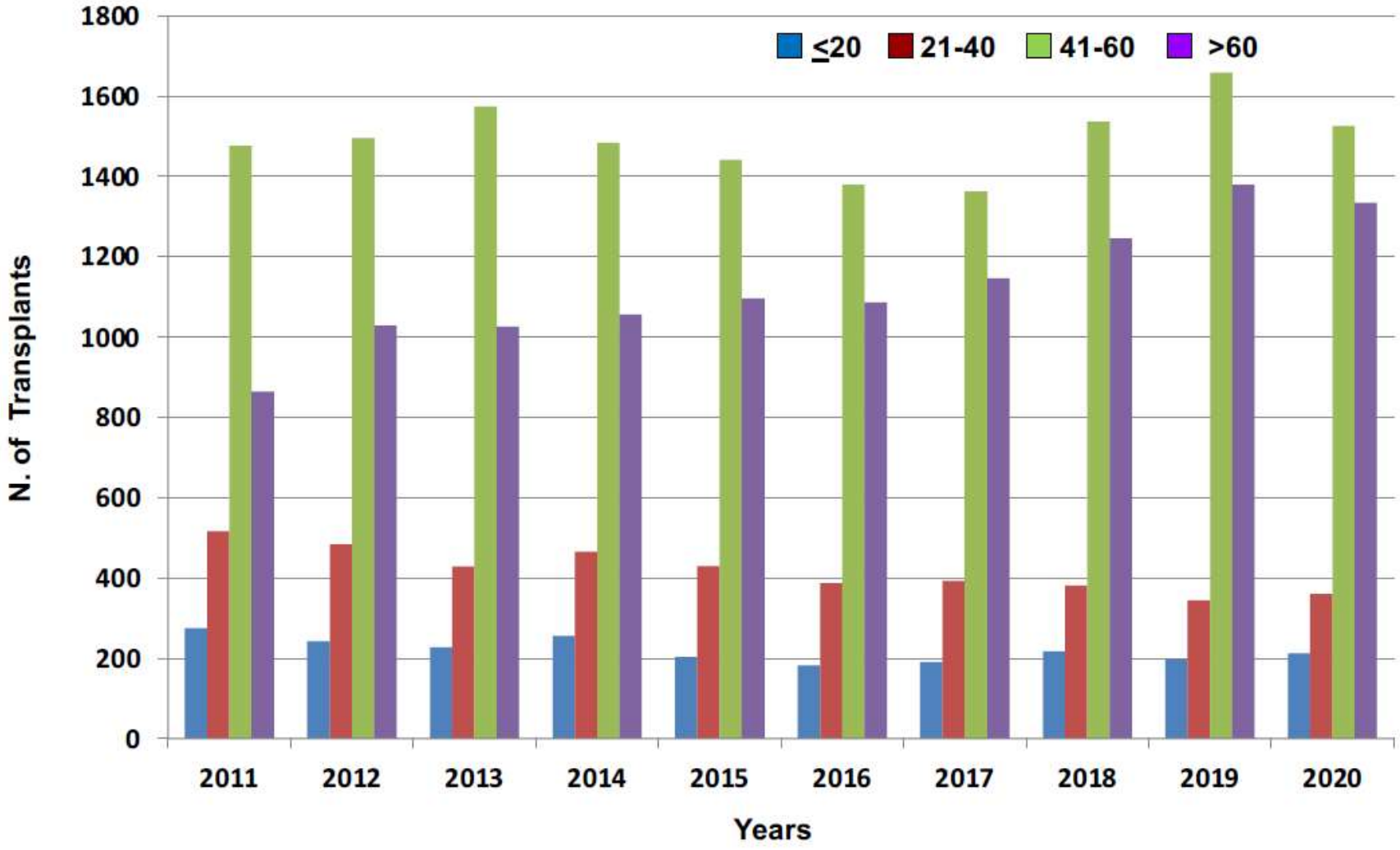
Autologous Transplants - Indications 2019



Export date 06/03/2020

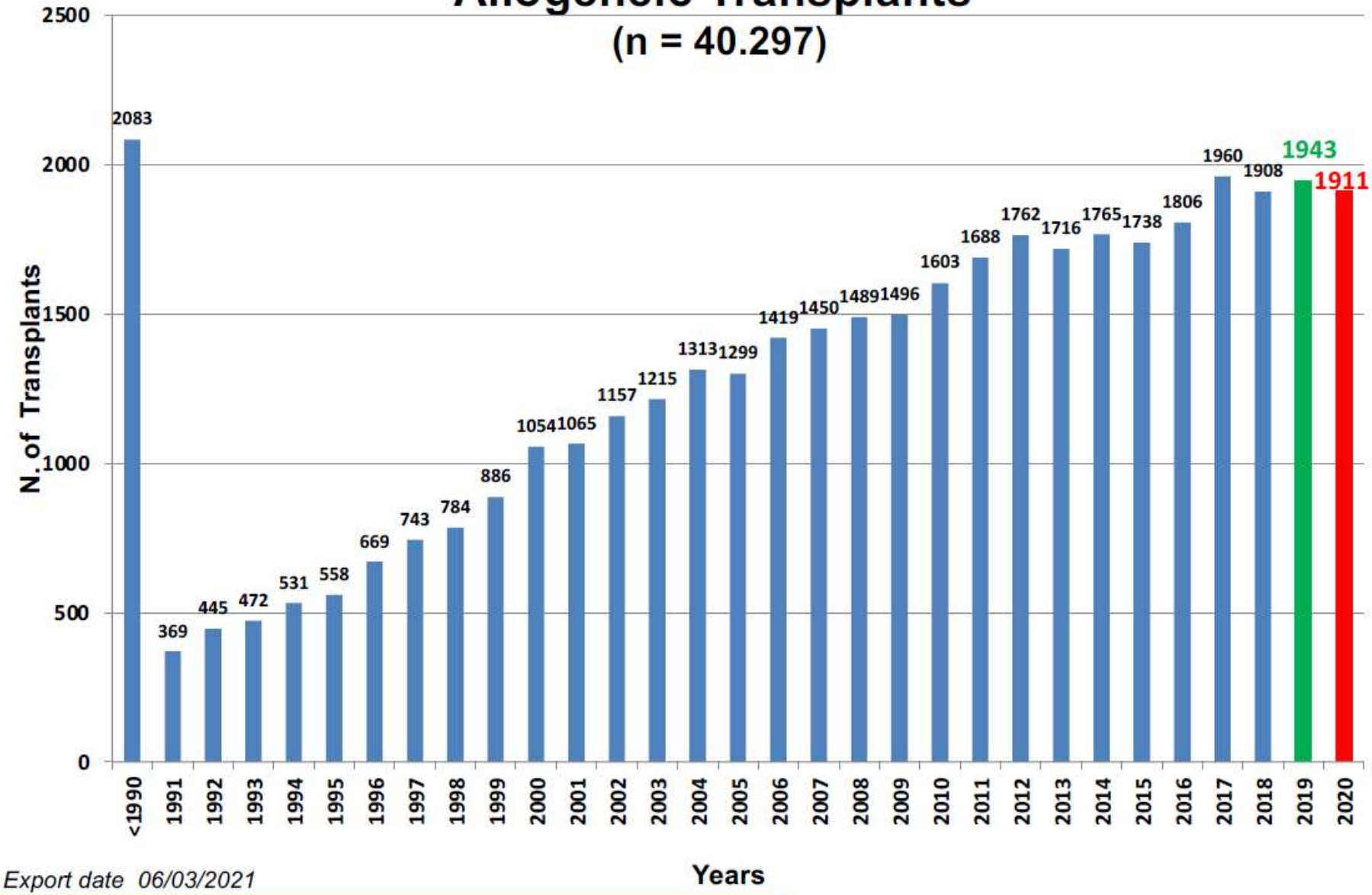
GITMO

Autologous Transplants – Patient age at transplantation



Export date 06/03/2021

Allogeneic Transplants
(n = 40.297)

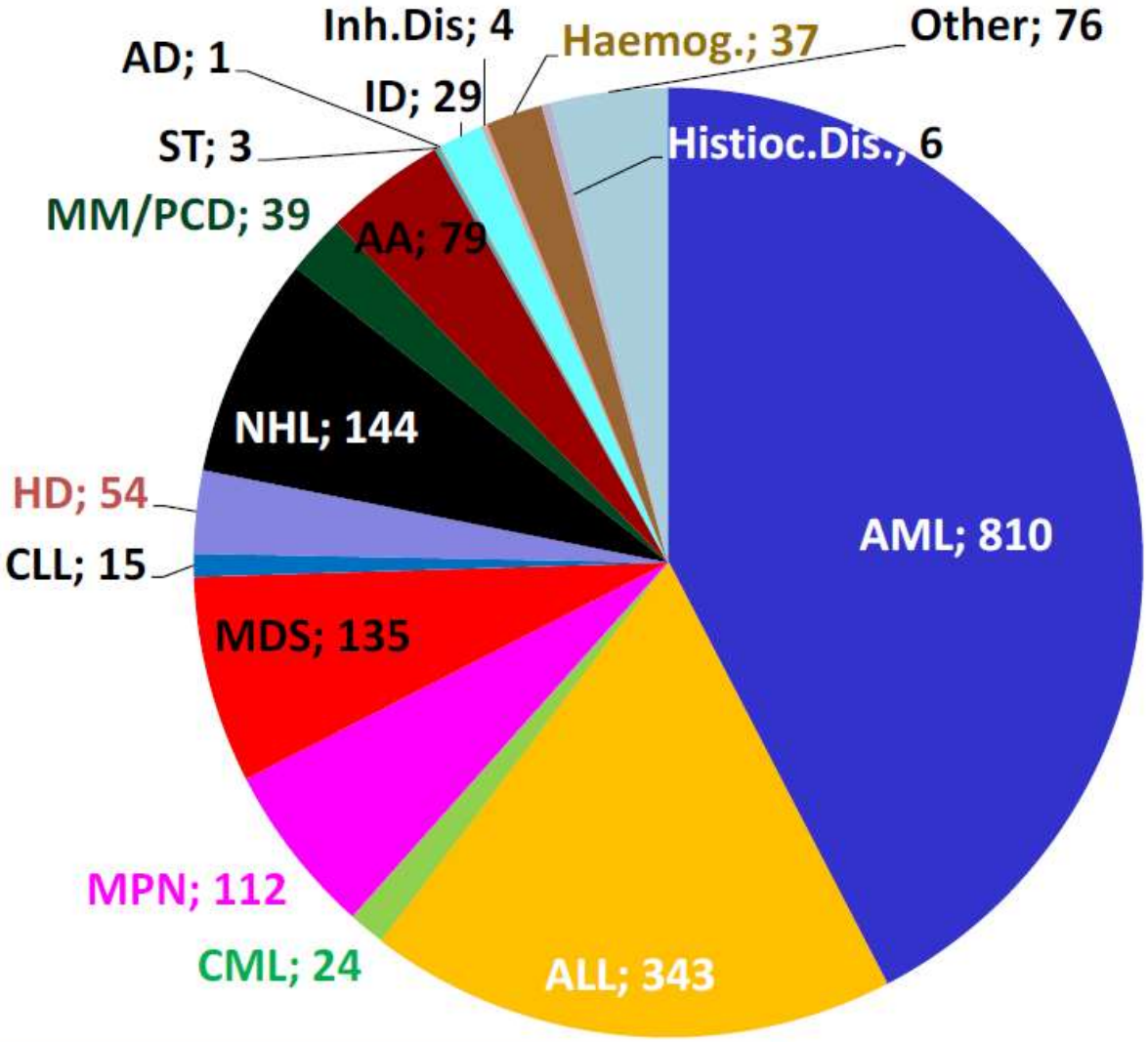


Export date 06/03/2021

DA VITA NASCE VITA: PROMUOVERE LA DONAZIONE DI CELLULE STAMINALI EMOPOIETICHE IN ITALIA

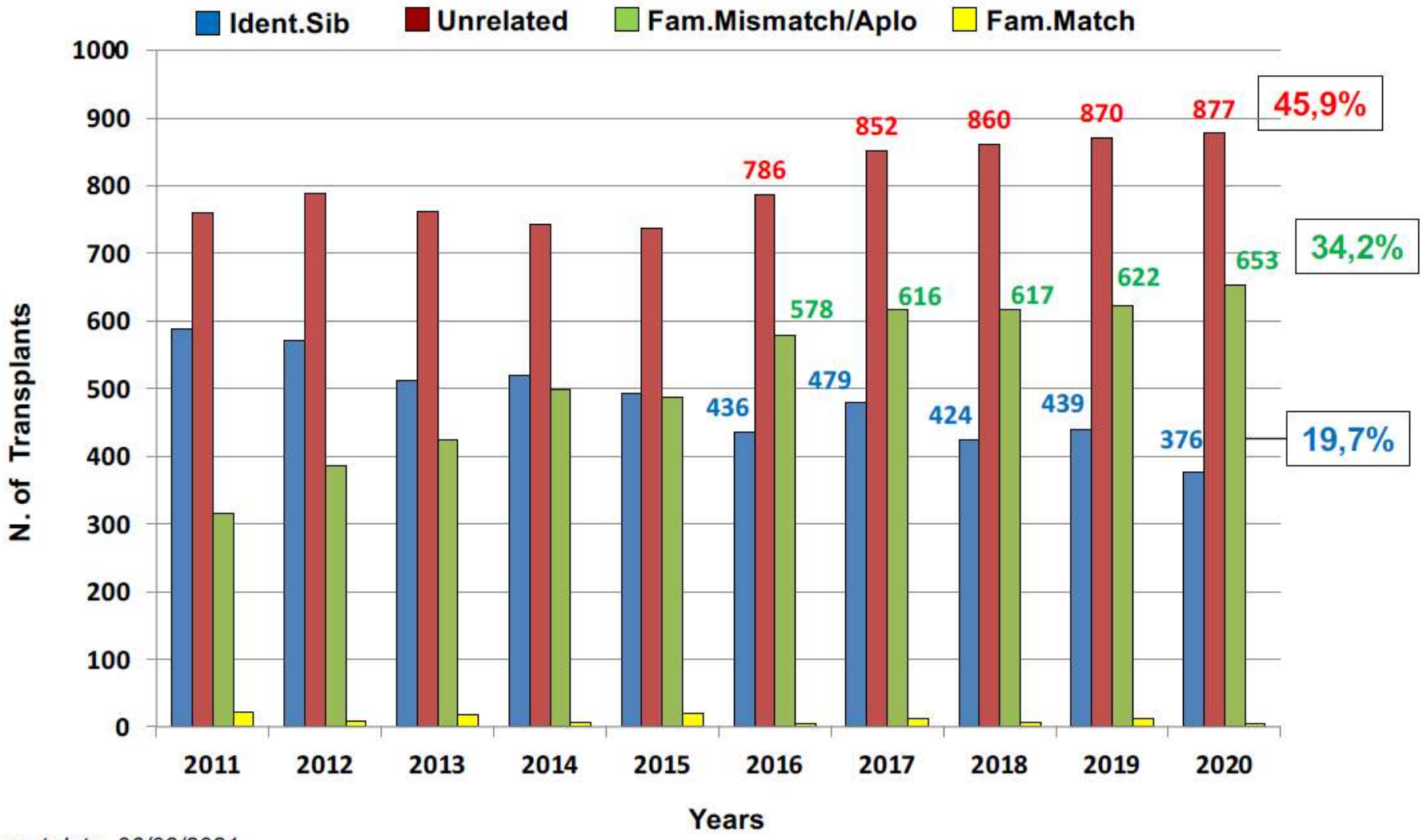
GITMO

Allogeneic Transplants - Indications 2020



GITMO

Allogeneic Transplants – Donor type



Export date 06/03/2021

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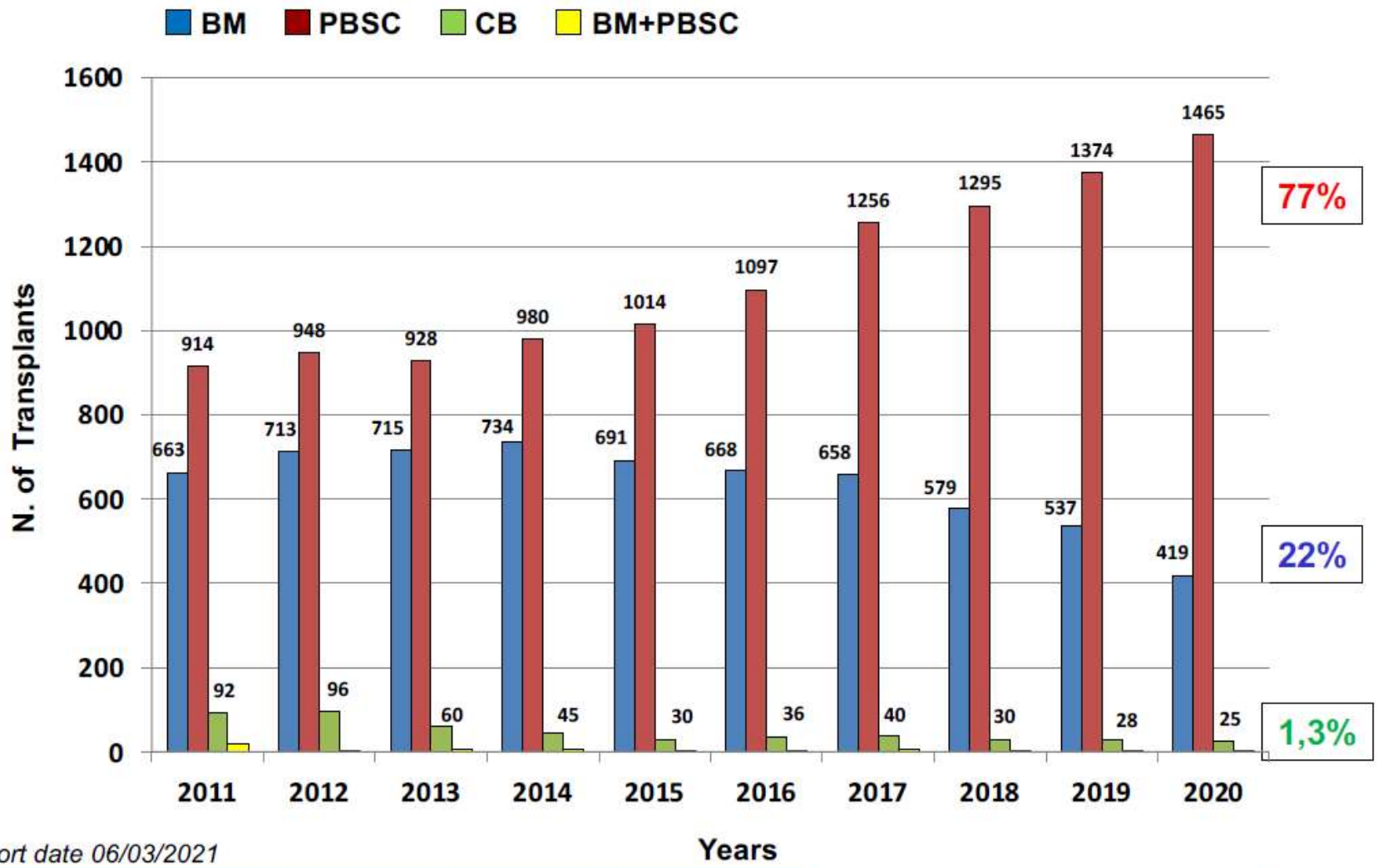
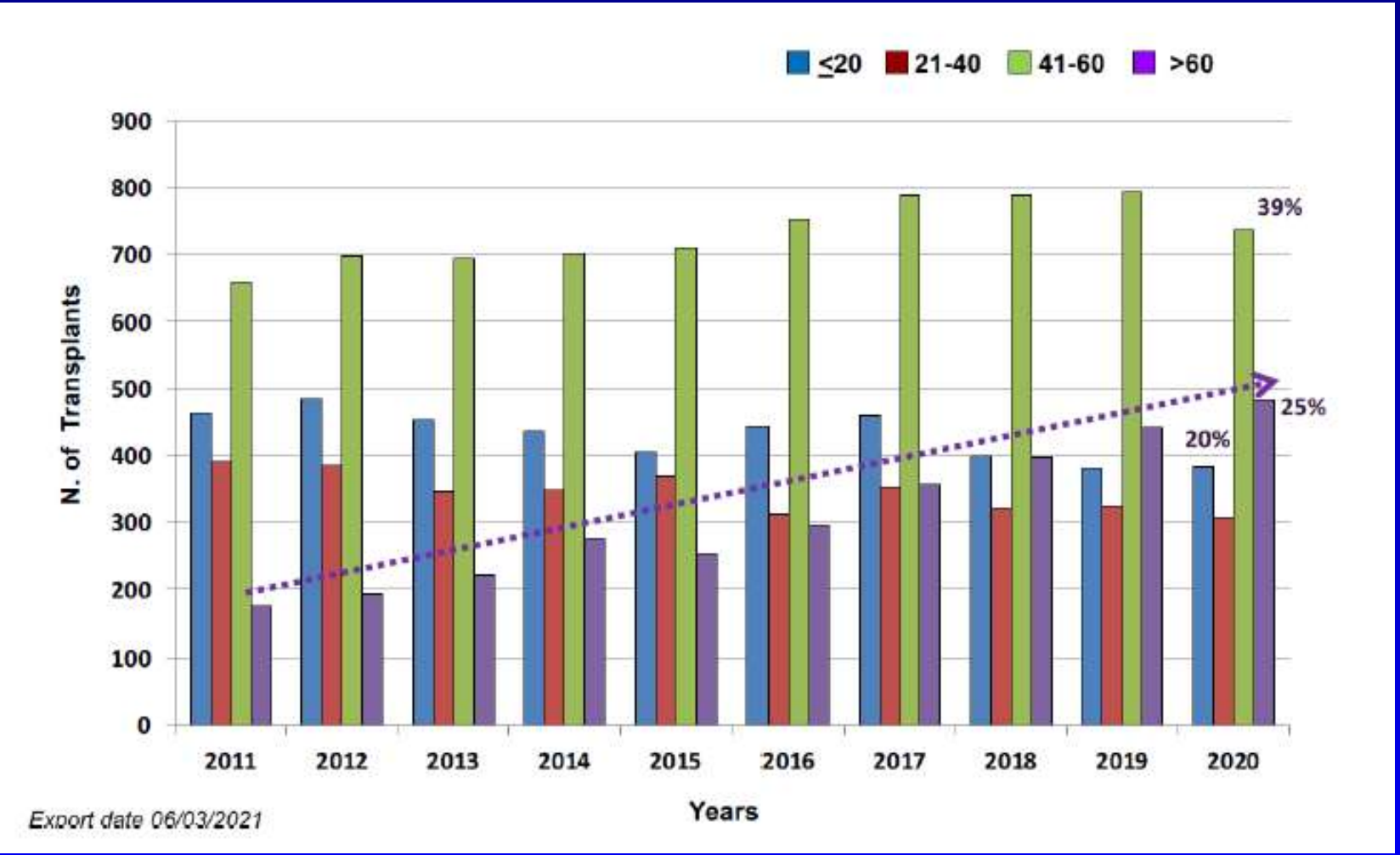
Allogeneic Transplants – Source of HSC

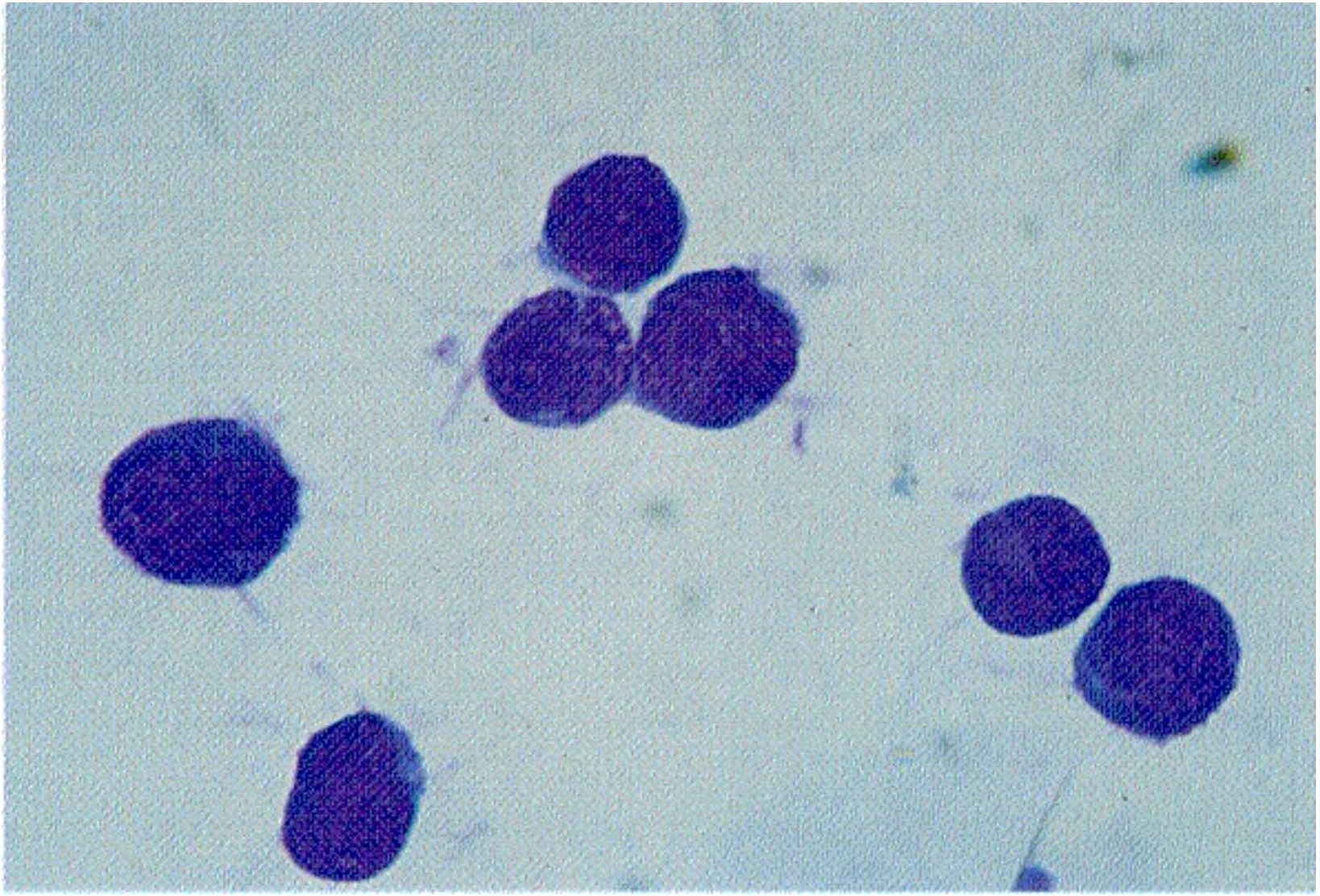


Export date 06/03/2021

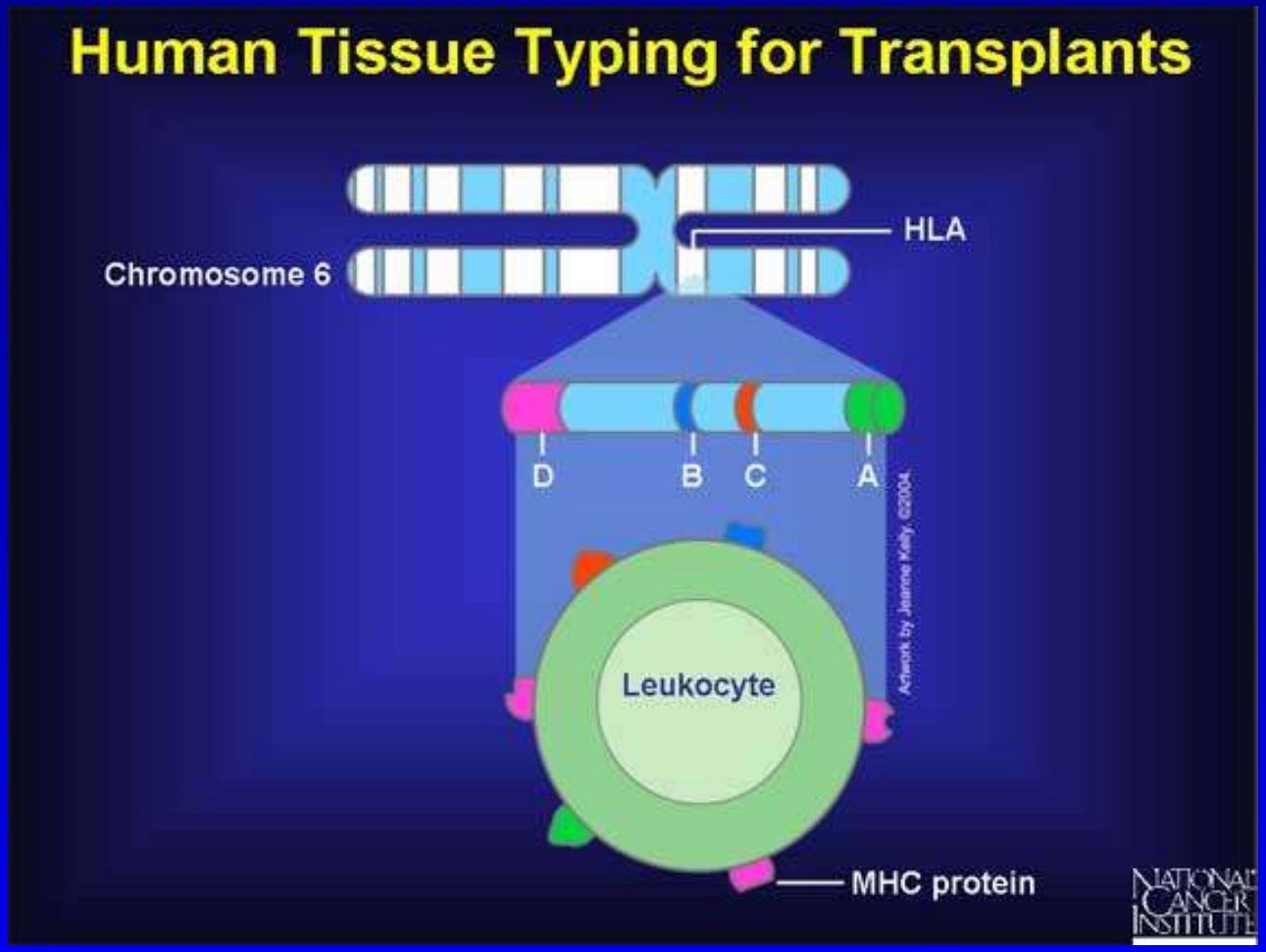
GITMO

TRAPIANTI ALLOGENICI IN ITALIA

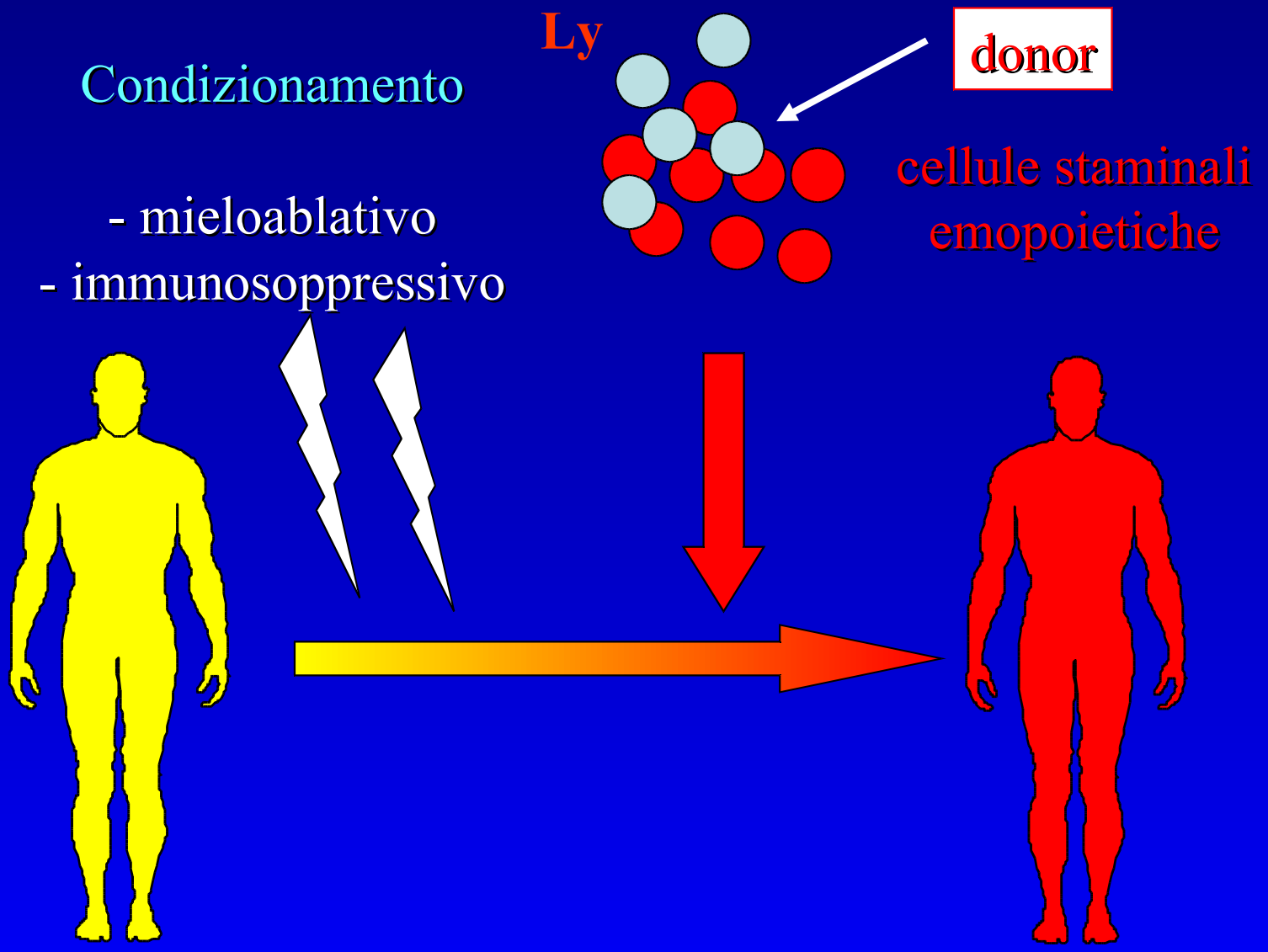




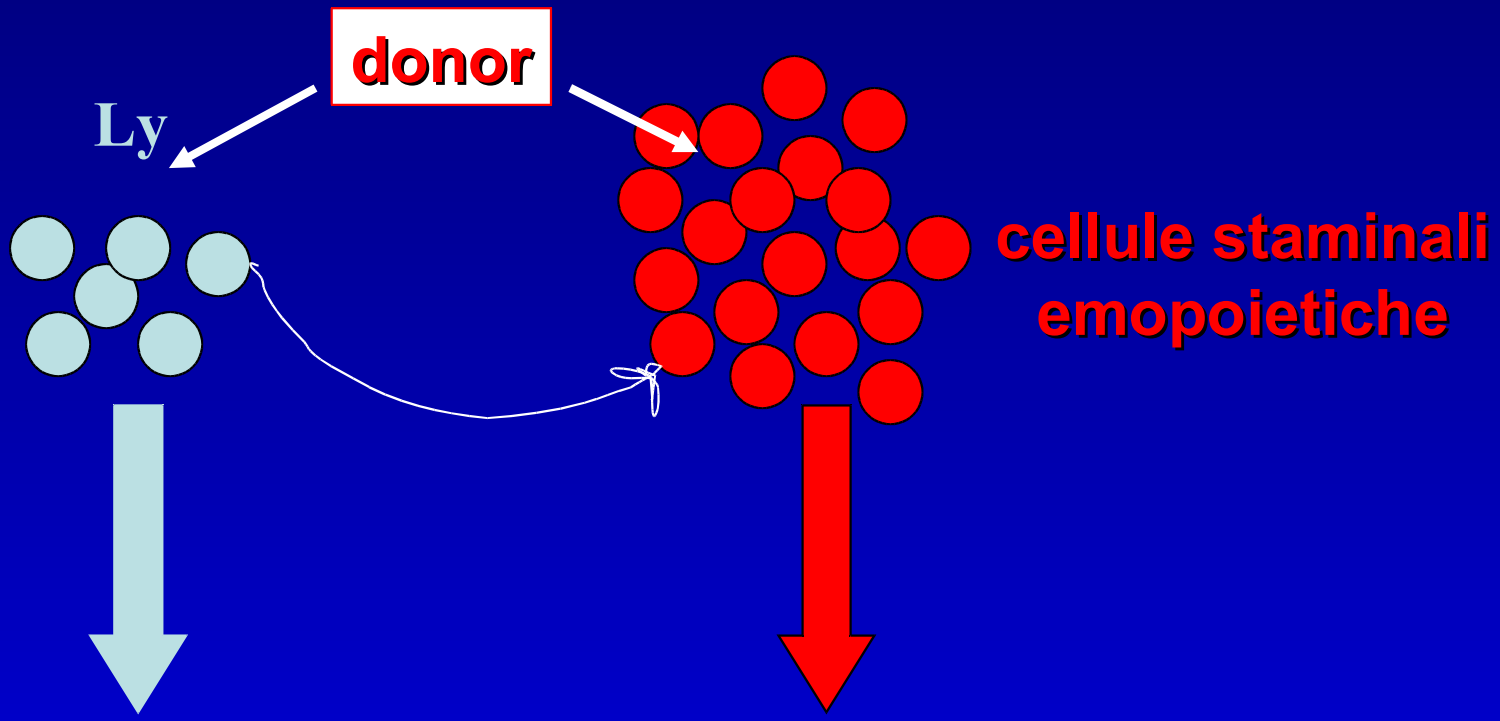
Trapianto di CSE allogeniche e sistema HLA



Trapianto allogenico di cellule staminali emopoietiche



Trapianto allogenico di cellule staminali emopoietiche



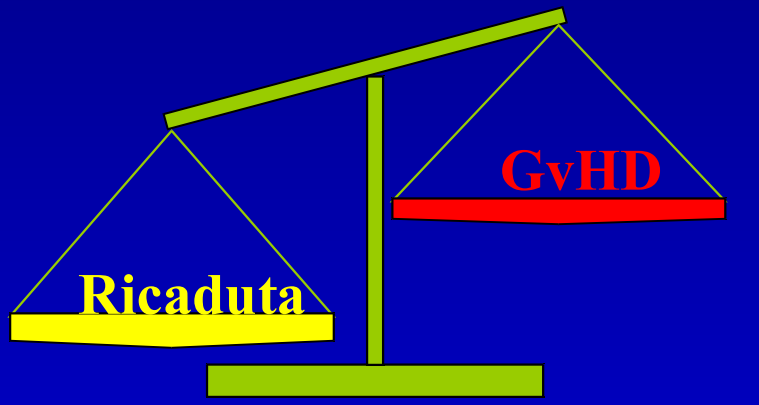
effetto anti-tumorale (GVL)

ricostituzione emopoietica

Transplant Related Mortality (TRM)

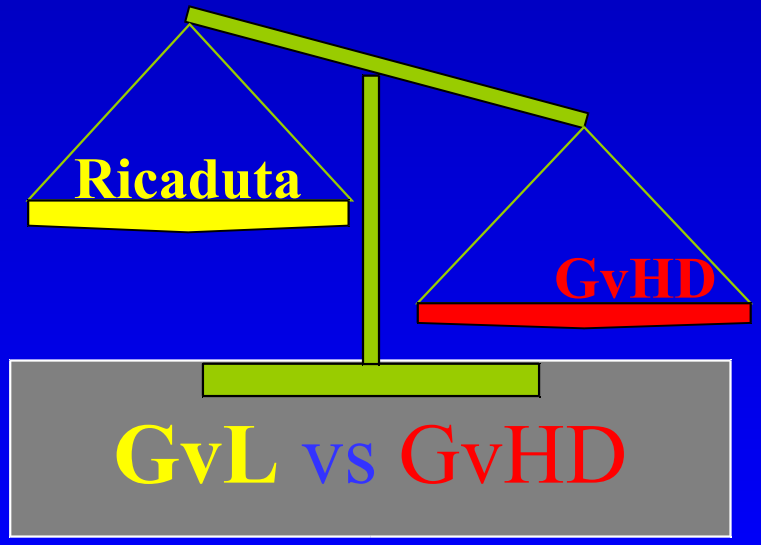
reazione del trapianto verso l'ospite (GVHD)

Graft-*versus*-Host reaction



Minore GvHD - GVL

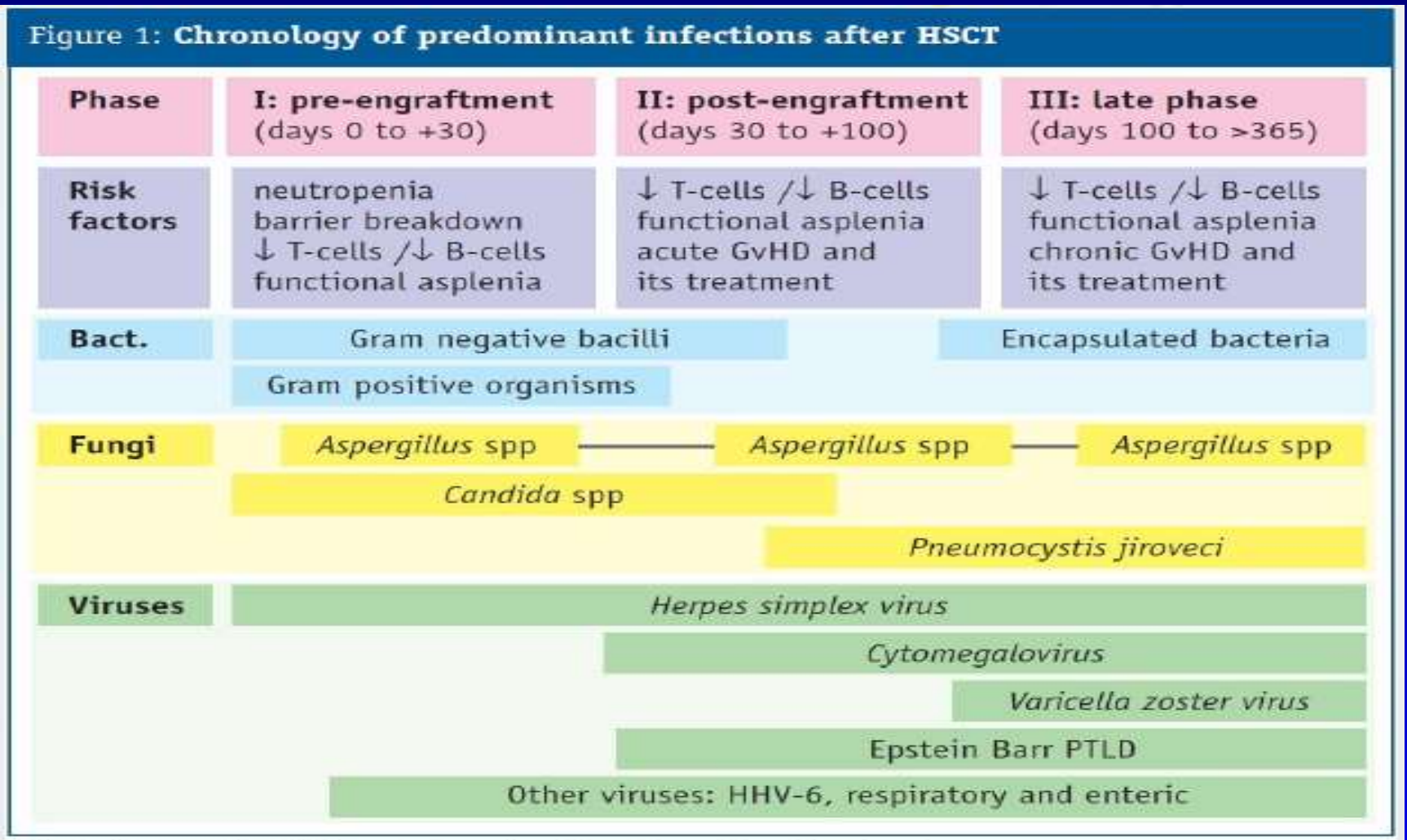
Maggiore prob. di ricaduta



Maggiore GvHD + GVL

Minore prob. di ricaduta

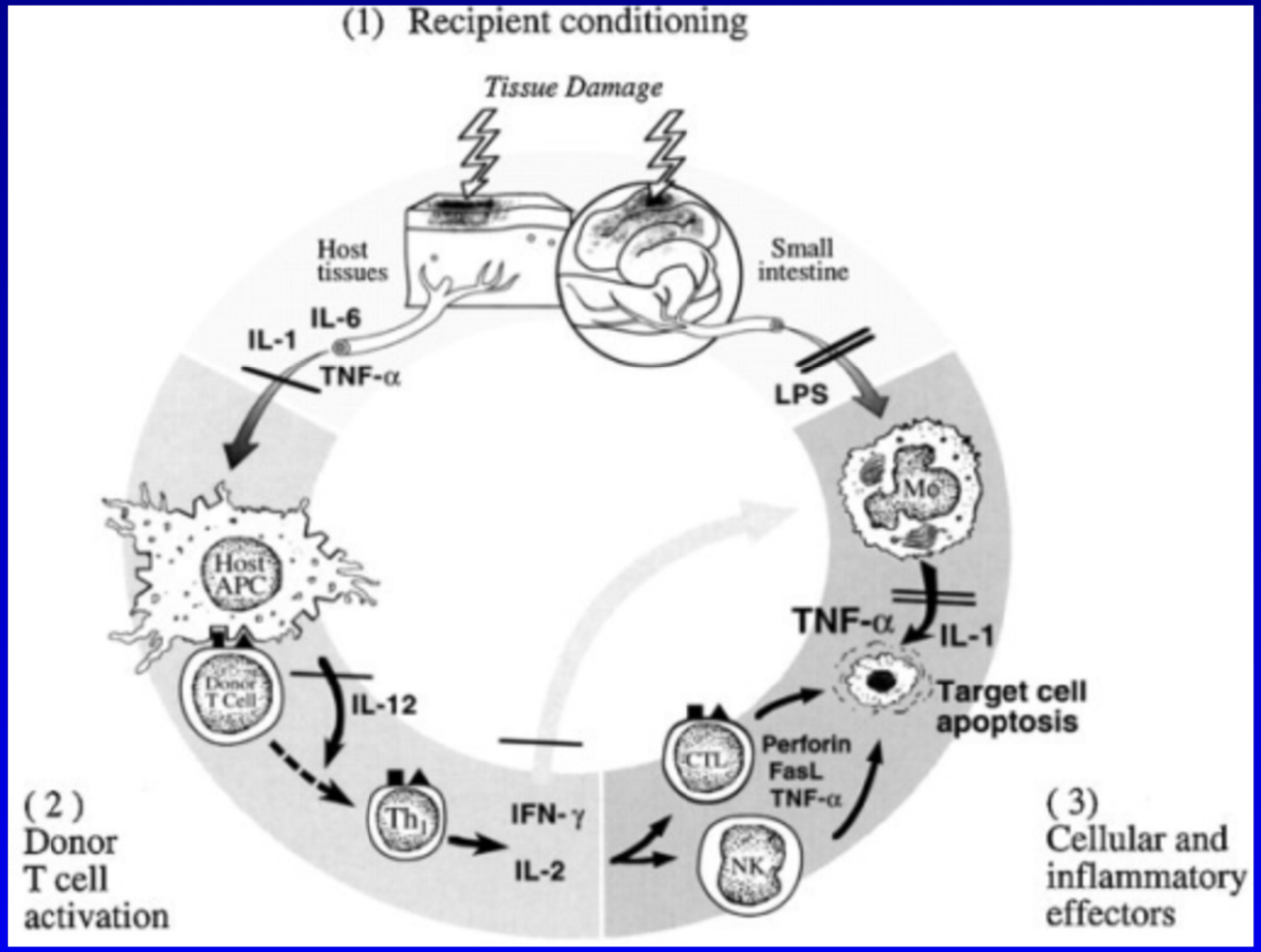
Figure 1: **Chronology of predominant infections after HSCT**



Adapted from (2). PTLD: post-transplant lymphoproliferative disorder

Kedia S, Acharya PS, Mohammad F, Nguyen H, Asti D, Mehta S, Pant M, Mobarakai M. Infectious complication of hematopoietic stem cell transplantation. J Stem Cell Res Ther2013, S3

PATHOPHYSIOLOGY OF aGVHD



Staging and Grading of aGVHD

Acute GVHD	Organ Involvement: Skin	Organ Involvement: Liver, Bilirubin Level, mg/dL	Organ Involvement: Gastrointestinal Tract
Stage			
1+	Erythematous rash <25% of BSA	2-3	Diarrhea >500 mL/d or persistent nausea
2+	Erythematous rash 25%-50% of BSA	4-6	Diarrhea >1000 mL/d
3+	Erythematous rash >50% of BSA, and erythroderma	7-15	Diarrhea >1500 mL/d
4+	Generalized erythroderma with bulla formation	>15	Severe abdominal pain with or without ileus
Grade			
I	1+ to 2+	0	0
II	1+ to 3+	1+	1+
III	2+ to 3+	2+ to 3+	2+ to 4+
IV	4+	4+	NA

Abbreviations: BSA, body surface area; GVHD, graft-vs-host disease; NA, not available.

*Data from Przepiorka et al.[4]

FIRST-LINE SYSTEMIC THERAPY of aGVHD (grade ≥ 2)

6-Methylprednisolone 2 mg/Kg/day (*1 mg/Kg/day in grade II isolated aGVHD?*)

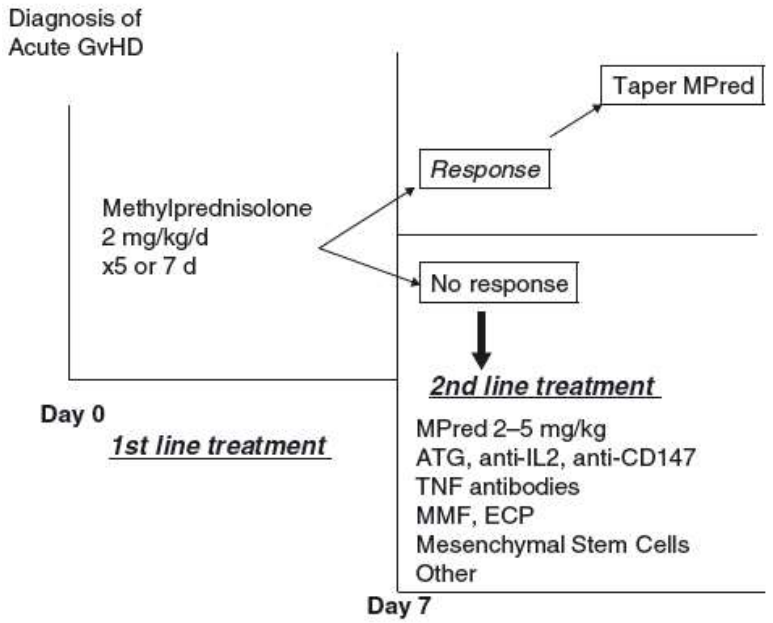
TAPERING → NO consensus

After response evaluation (5-7 days), if aGVHD under good control

↓

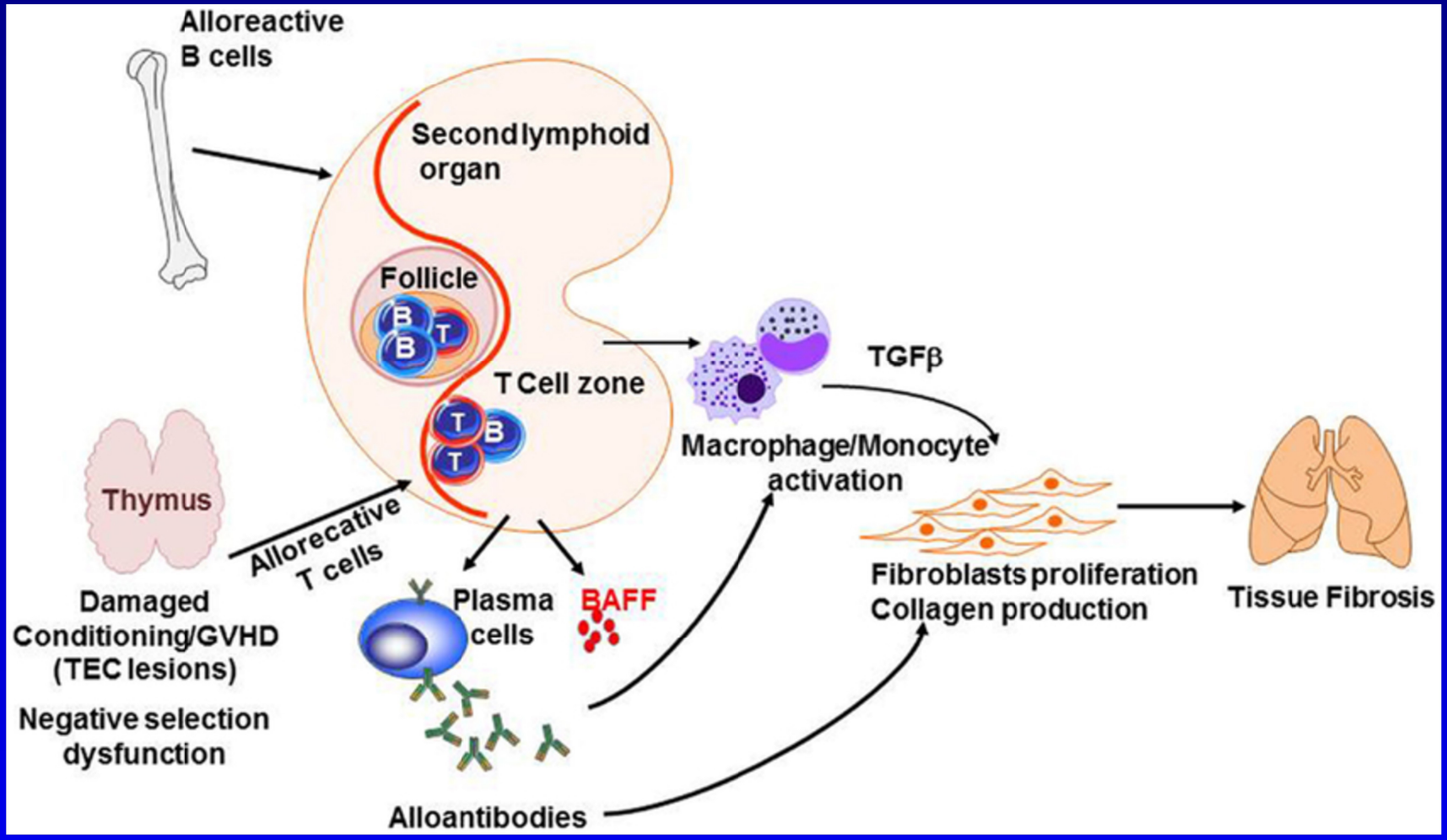
0,2 mg/Kg/day every 3-5 days

Martin PJ et al, BBMT 2009



Bacigalupo A, BJH 2007

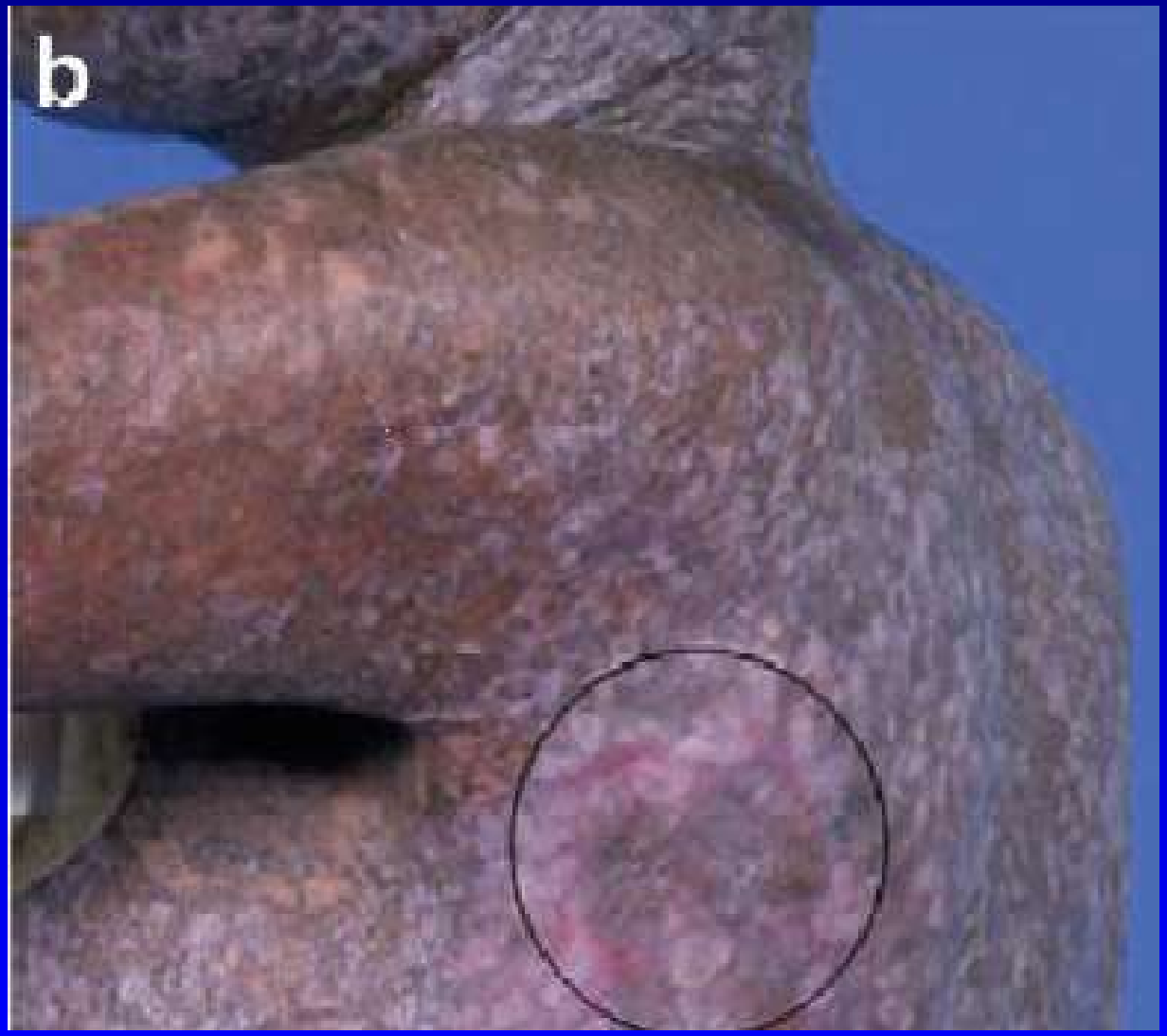
PATHOPHYSIOLOGY OF cGVHD



SIGNS & SYMPTOMS of Chronic GVHD

ORGAN/SITE	
SKIN	Erythema, maculopapular rash, pruritus, poikiloderma, lichen-like features
NAILS	dystrophy
SCALP	alopecia
MOUTH	Lichen, xerostomia, mucositis
EYES	Keratoconjunctivitis sicca, photophobia, blepharitis
GI tract	Strictures of oesophagus, anorexia, weight loss
LIVER	Bilirubin or ALP > 2 x ULN
LUNG	BOS
MUSCLES, JOINTS	Fascitis, joint contractures, myositis, cramps, arthralgias
HEMATOPOIETIC & IMMUNE	Thrombocytopenia, eosinophilia, lymphopenia
OTHER	Ascites, pericardial or pleural effusion

cGVHD



cGVHD

Chronic GVHD

Chronic GVHD

Chronic GVHD

Chronic GVHD

Chronic GVHD

Scoring of cGVHD

cGVHD: NIH Global Scoring

- Mild
  - No significant impairment of function
  - Only 1 or 2 organs (except lung)
  - Maximum organ score of 1
- Moderate
  - Significant impairment but no major disability
  - 3 or more organs with maximum score of 1
  - One organ with maximum score of 2
  - Lung score of 1
- Severe
  - Major disability
  - Score of 3 in any organ or site
  - Lung score >2

FIRST-LINE SYSTEMIC THERAPY of cGVHD

Drug	Level of recommendation/ evidence		Response
	Grade	Evidence	
Steroids (0.5–1.0 mg/kg/day)	A	I	**CR: 30–50%**
Steroids + CNI[1–3]	C-1	II	**CR: 30–50%**

High-risk cGvHD: 3-year OS was 26% when using steroids as a single agent; the combination with CsP increased survival to 52%

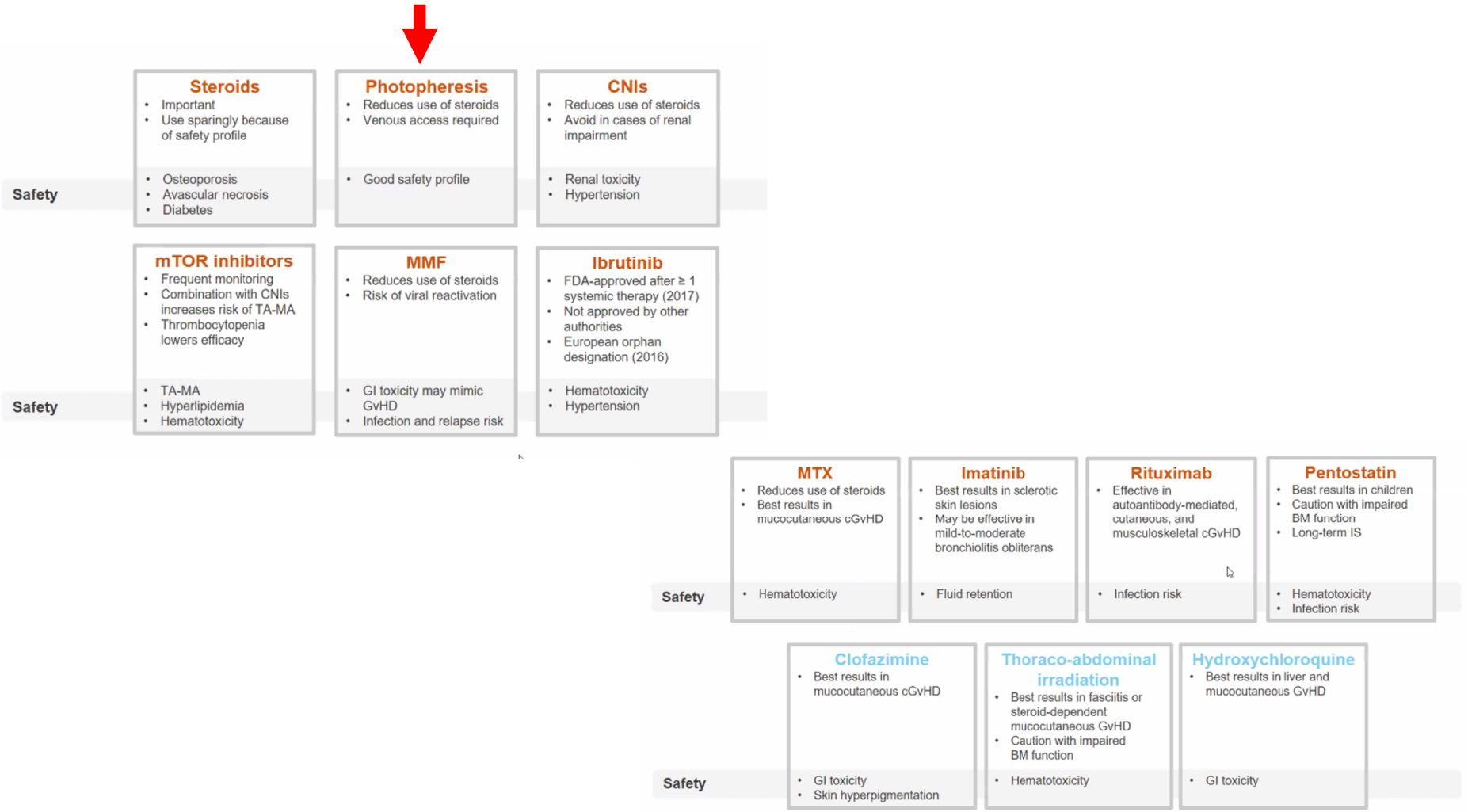
Standard-risk cGvHD: addition of CsP to systemic IS did not increase survival, although it may reduce the risk for steroid-related toxicity

A = It should always be used.
C-1 = Its use is justified in 1st line.
I = Evidence of randomized controlled study.
II = Evidence of > 1 well-designed but not randomized clinical trial.

CR, complete response; CsP, cyclosporine; OS, overall survival.

1. Koc S, et al. *Blood*. 2002;100:48-51.
2. Sladak M, Sullivan KM. *Blood Rev*. 1994;8:154-60.
3. Sullivan KM, et al. *Blood*. 1988;72:555-61.

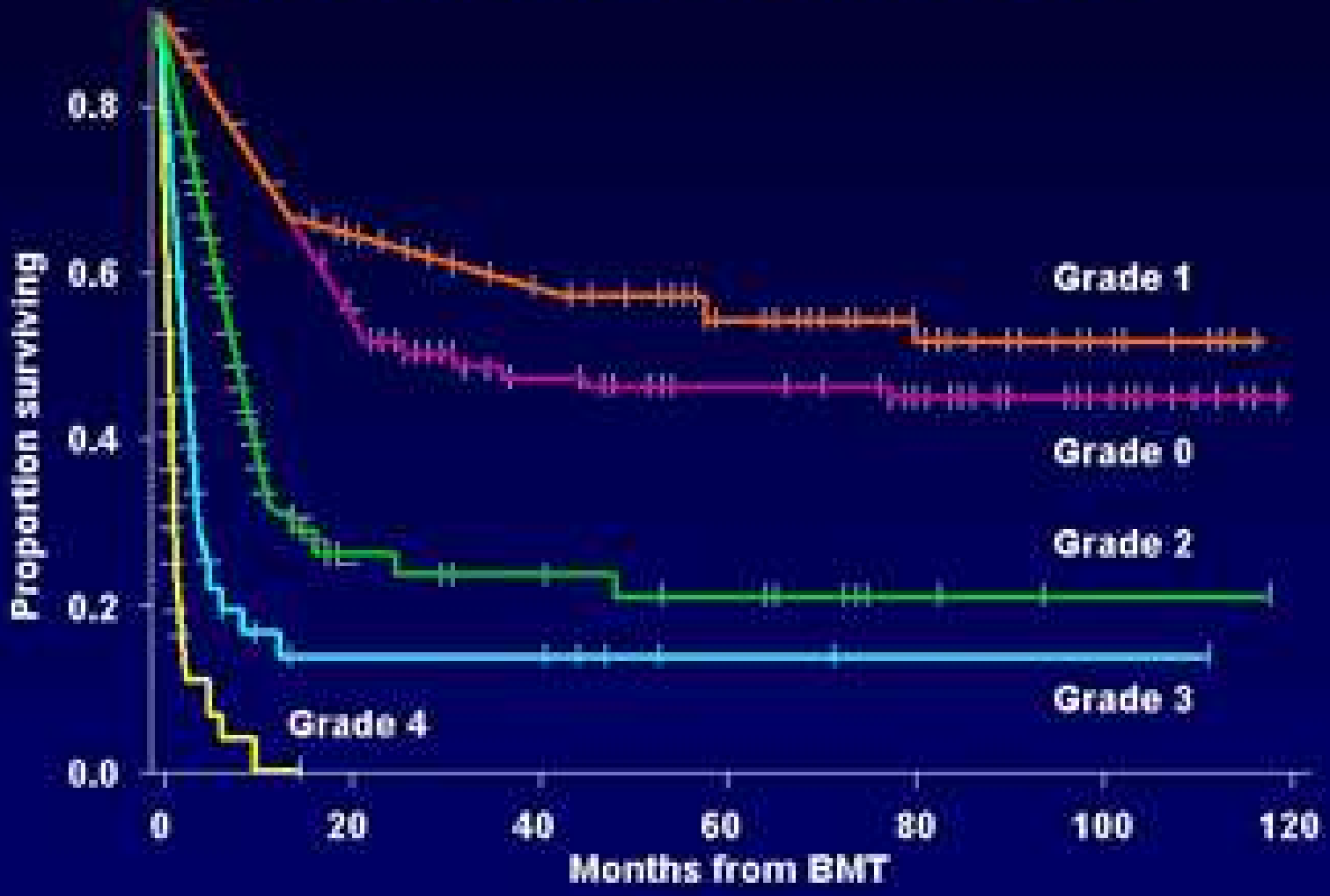
2nd LINE THERAPY FOR SR-cGVHD



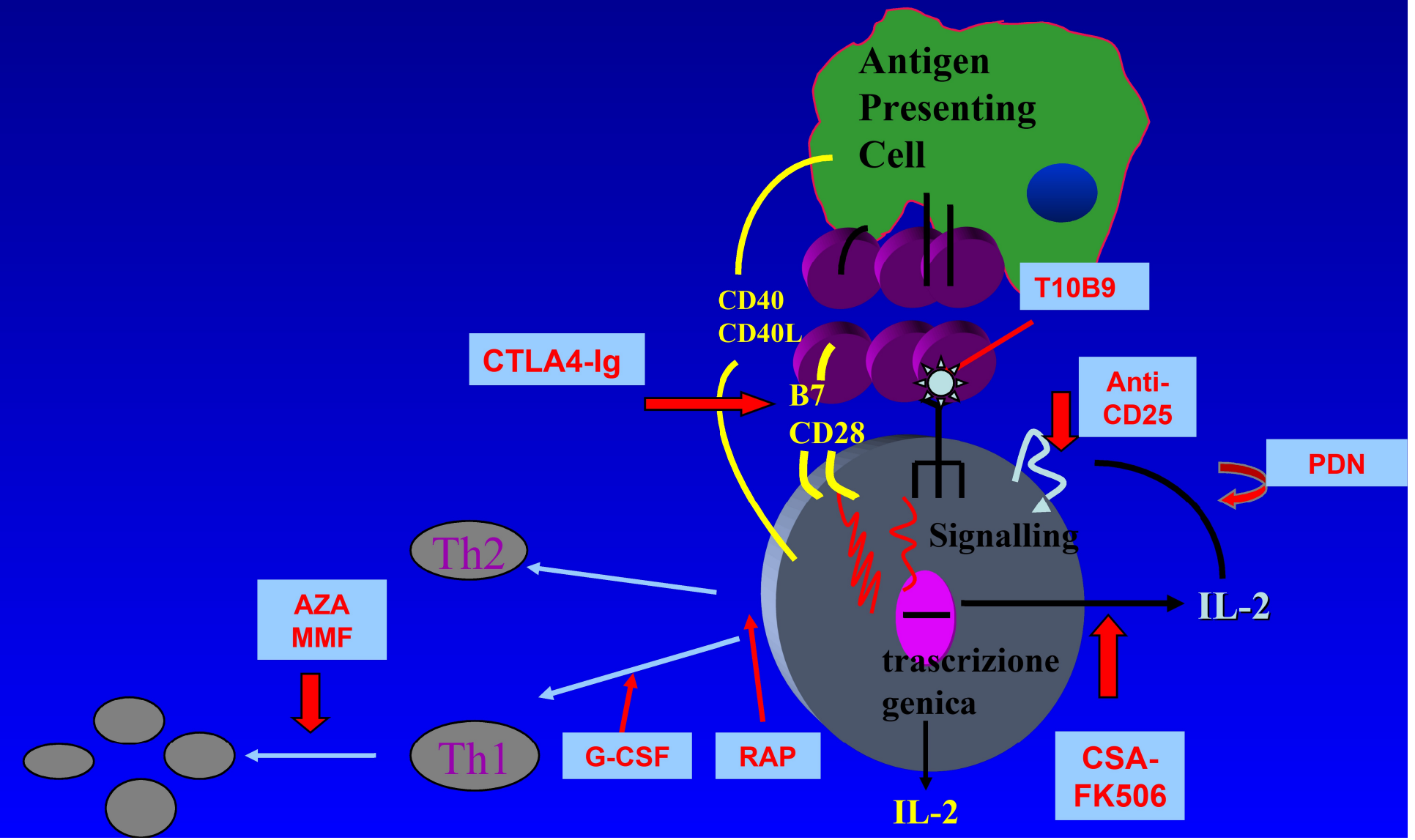
Cutler C et al. *Blood*. 2006;108:756-62. Duarte RF et al. *Bone Marrow Transplant*. 2014;49:49-54. Jaglowski SM, Blazar BR. *Blood Adv*. 2018;2:2012-9
Martin PJ et al. *Biol Blood Marrow Transplant*. 2012;18:1150-63. Miklos D et al. *Blood*. 2017;130:2243-50
Ruutu T et al. *Bone Marrow Transplant*. 2014;49:168-73. Wolff D et al. *Biol Blood Marrow Transplant*. 2011;17:1-17

Cutler C et al. *Blood*. 2006;108:756-62. Jaglowski SM, Blazar BR. *Blood Adv*. 2018;2:2012-9
Martin PJ et al. *Biol Blood Marrow Transplant*. 2012;18:1150-63. Miklos D et al. *Blood*. 2017;130:2243-50
Ruutu T et al. *Bone Marrow Transplant*. 2014;49:168-73. Wolff D et al. *Biol Blood Marrow Transplant*. 2011;17:1-17

Survival After Allogeneic BMT

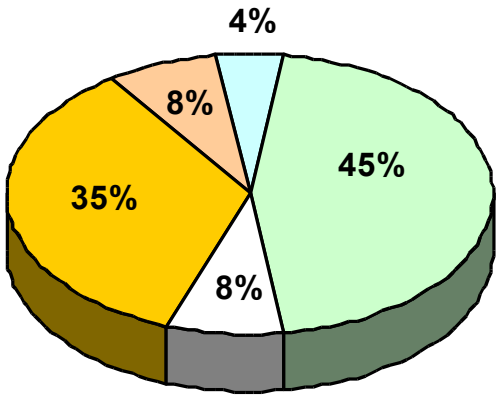


GVHD

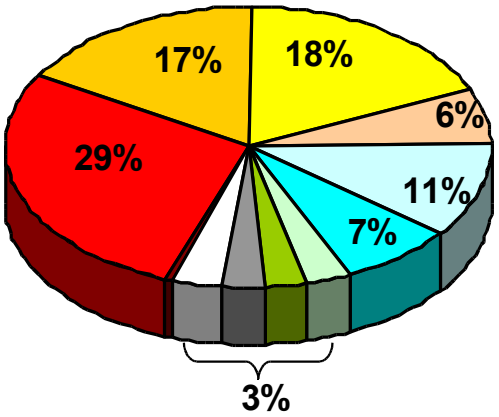

Antigen
Presenting
Cell
T10B9
CD40
CD40L
CTLA4-Ig
B7
CD28
Anti-
CD25
PDN
Signalling
IL-2
trascrizione
genica
Th2
AZA
MMF
Th1
G-CSF
RAP
CSA-
FK506
IL-2

Patologie dei pazienti in ricerca

Patologie dei pazienti in ricerca nel 1990



Patologie dei pazienti in ricerca nel 2009



- Leucemia mieloide acuta
- Leucemia linfoblastica acuta
- Linfomi
- Mielodisplasia alto rischio
- Immunodeficienze e disordini congeniti
- Mieloma multiplo
- Leucemia mieloide cronica
- Talassemia
- Mielofibrosi idiopatica
- Anemia aplastica severa
- Neuroblastoma

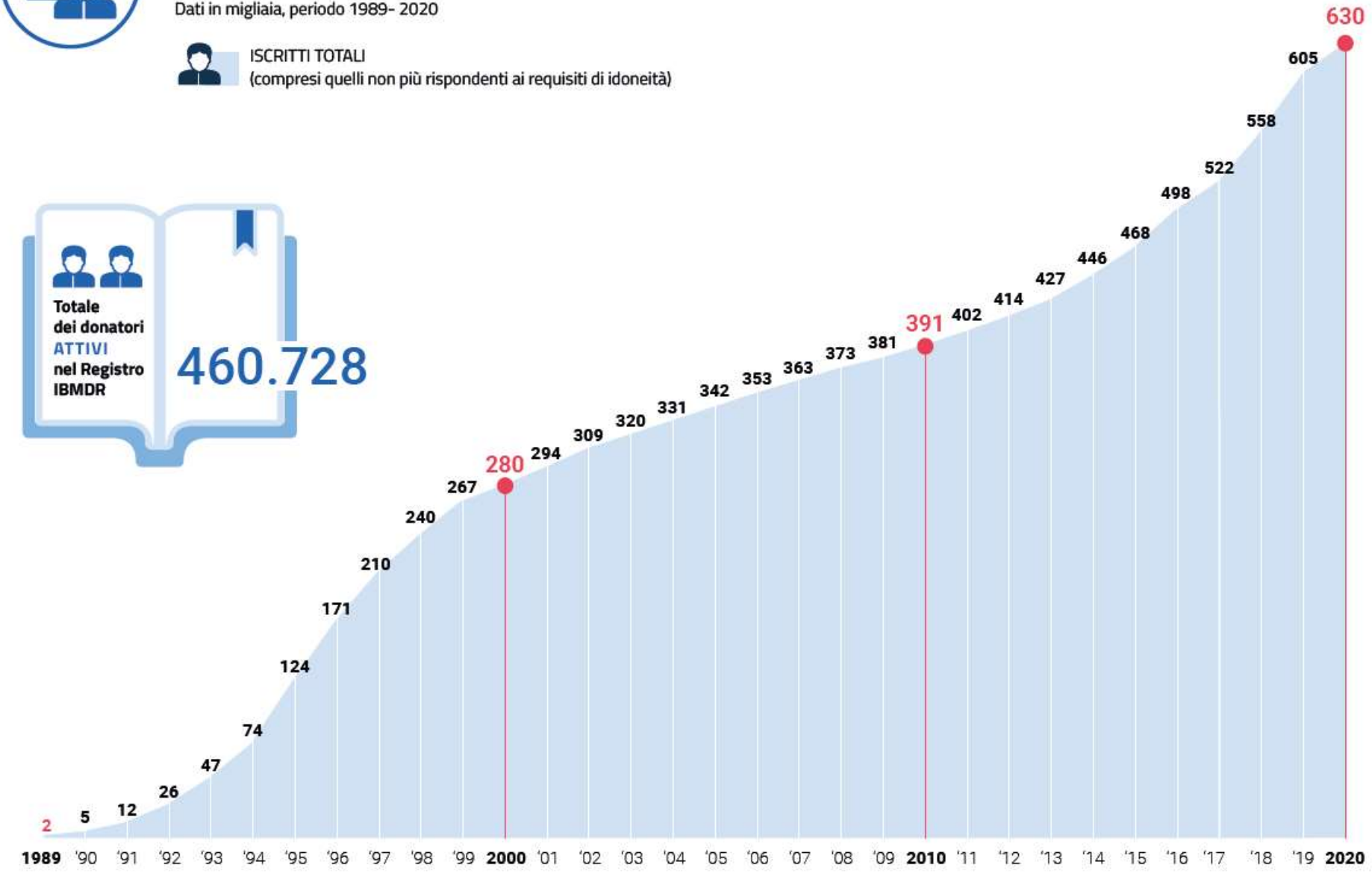
DONATORI ISCRITTI AL REGISTRO IBMDR

Dati in migliaia, periodo 1989- 2020

ISCRITTI TOTALI
(compresi quelli non più rispondenti ai requisiti di idoneità)

Totale dei donatori ATTIVI nel Registro IBMDR

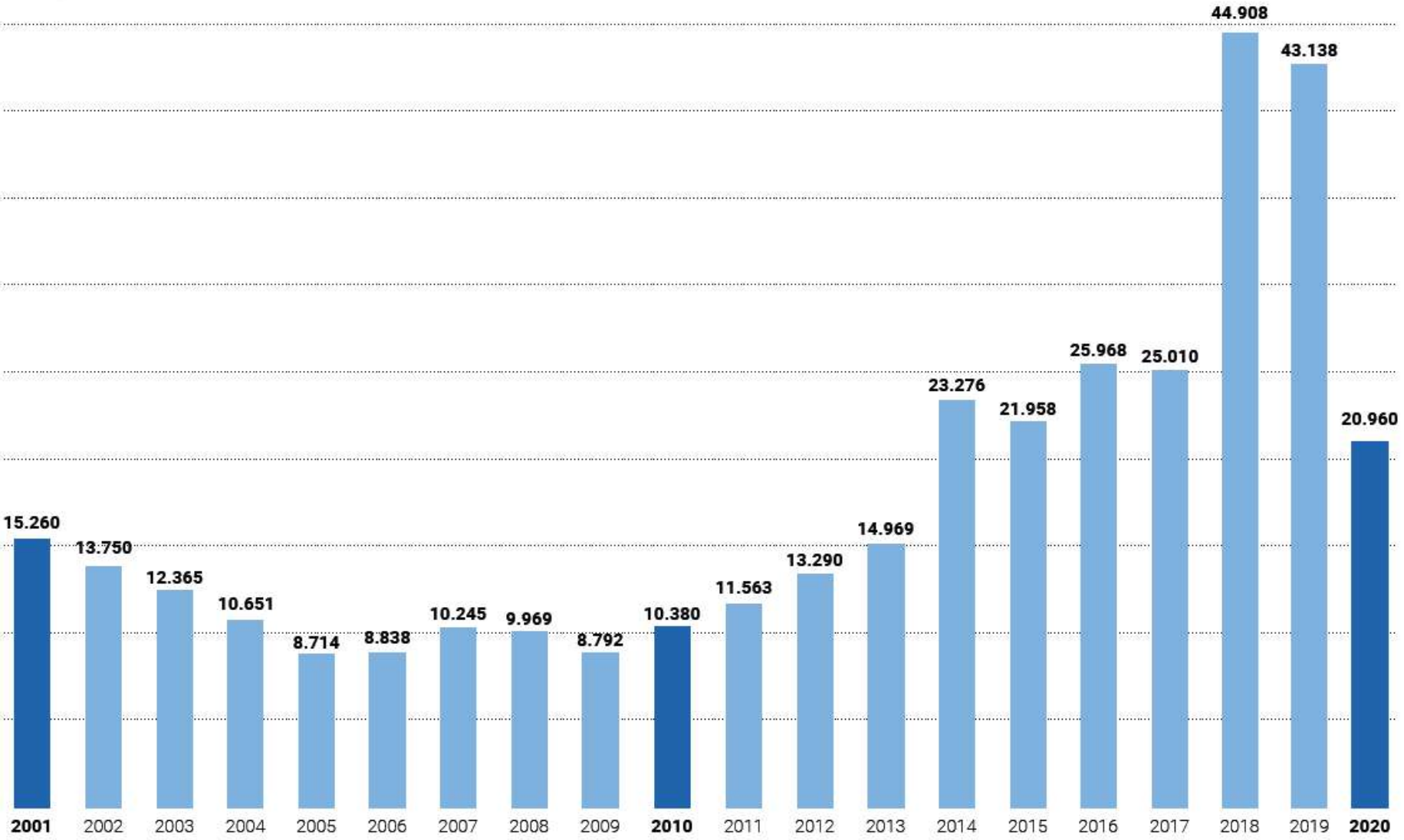
460.728



FONTE: REGISTRO IBMDR, DATI PRELIMINARI 2020

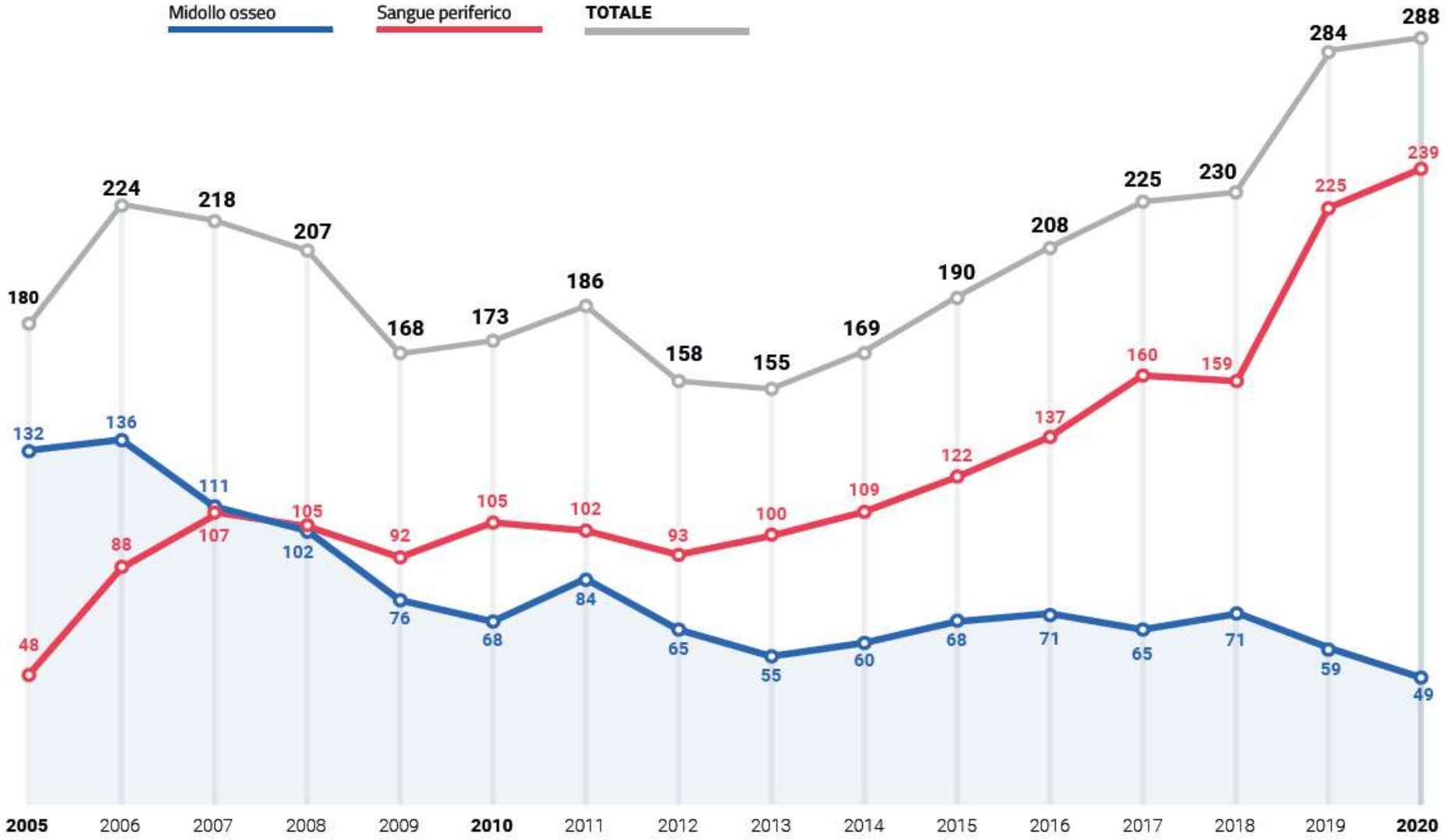
NUOVI ISCRITTI AL REGISTRO IBMDR

Andamento annuale



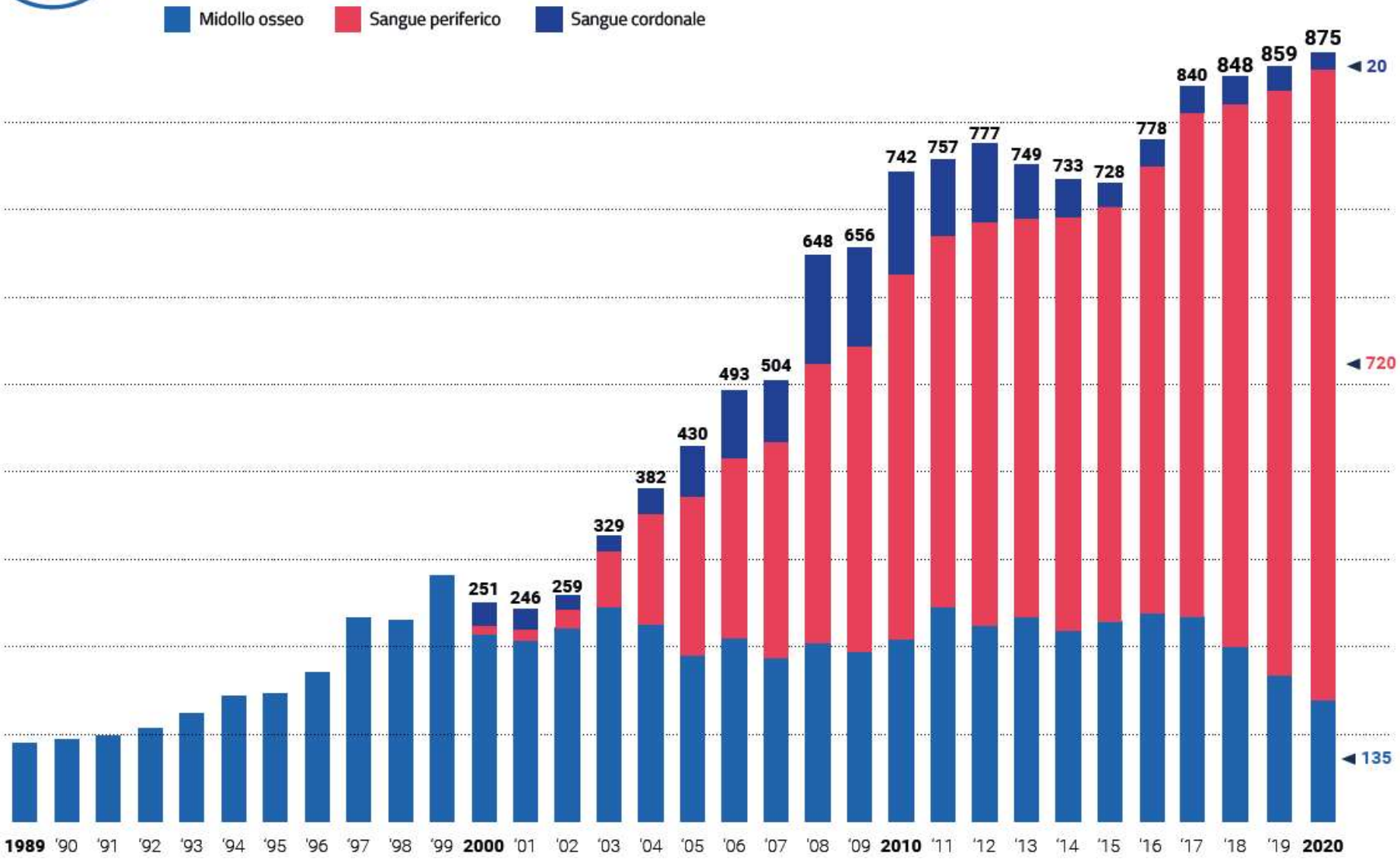
DONAZIONI DI CELLULE STAMINALI EMOPOIETICHE

Andamento annuale, dettaglio per sorgente



TRAPIANTI DI CELLULE STAMINALI EMOPOIETICHE

Da donatore non consanguineo



Banche e inventario unità sangue cordonale in Italia

Banca SCO	Inventario unità esposte 31 dicembre 2017
Bologna ER CBB	4.385
Calabria CBB	841
Campania CBB	1.762
Firenze CBB	2.276
Genova CBB	593
Lazio CBB	1.259
Milano CBB	10.403
Padova CBB	2.406
Pavia CBB	3.759
Pescara CBB	1.520
Pisa CBB	1.012
Puglia CBB	1.248
Sardegna CBB	136
Siacca CBB	41
Torino CBB	1.854
Treviso CBB	1.083
Unicatt CBB	559
Verona CBB	110
Totale	**35.247**

★ 18 Banche di unità di sangue cordonale (SCO) donate a scopo solidaristico della rete italiana ITCBN

PROBABILITA' DI IDENTIFICARE UN DONATORE