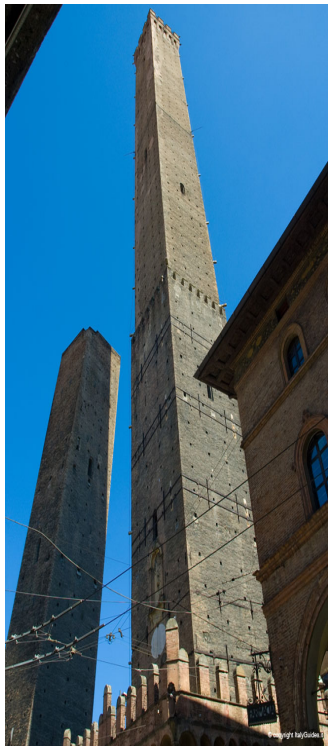
Transplantation trends in Italy: outcome and complications



FRANCESCA BONIFAZI

Hematology Dept.

University Hospital S. Orsola-Malpighi, Bologna

President of GITMO

GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

CUNEO May 17-19, 2018

GITMO

GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

THE NET

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

GITMO

GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

GITMO ACTIVITY 2017

GITMO Transplant Programs n= 95

Accredited n= 84

Non Accredited n= 11

	Accredited centers	ACCREDITATION		
		Autologous	Allogeneic	URD
Pediatric PT (n=10)	**9**	**9**	**9**	**9**
Adult PT (n=73)	**61**	**61**	**37**	**34**
Mixed PT (n=15)	**14**	**14**	**14**	**14**
TOTAL	**84**	**84**	**60**	**57**

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

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GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

REGULATORY ACTIVITY

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

MAJOR ISSUES

- ✓ The final document of the minimum requirements committee is in evaluation at the Conferenza Stato-Regione

- ✓ Transplant data flow will change: DPCM 15 marzo 2017

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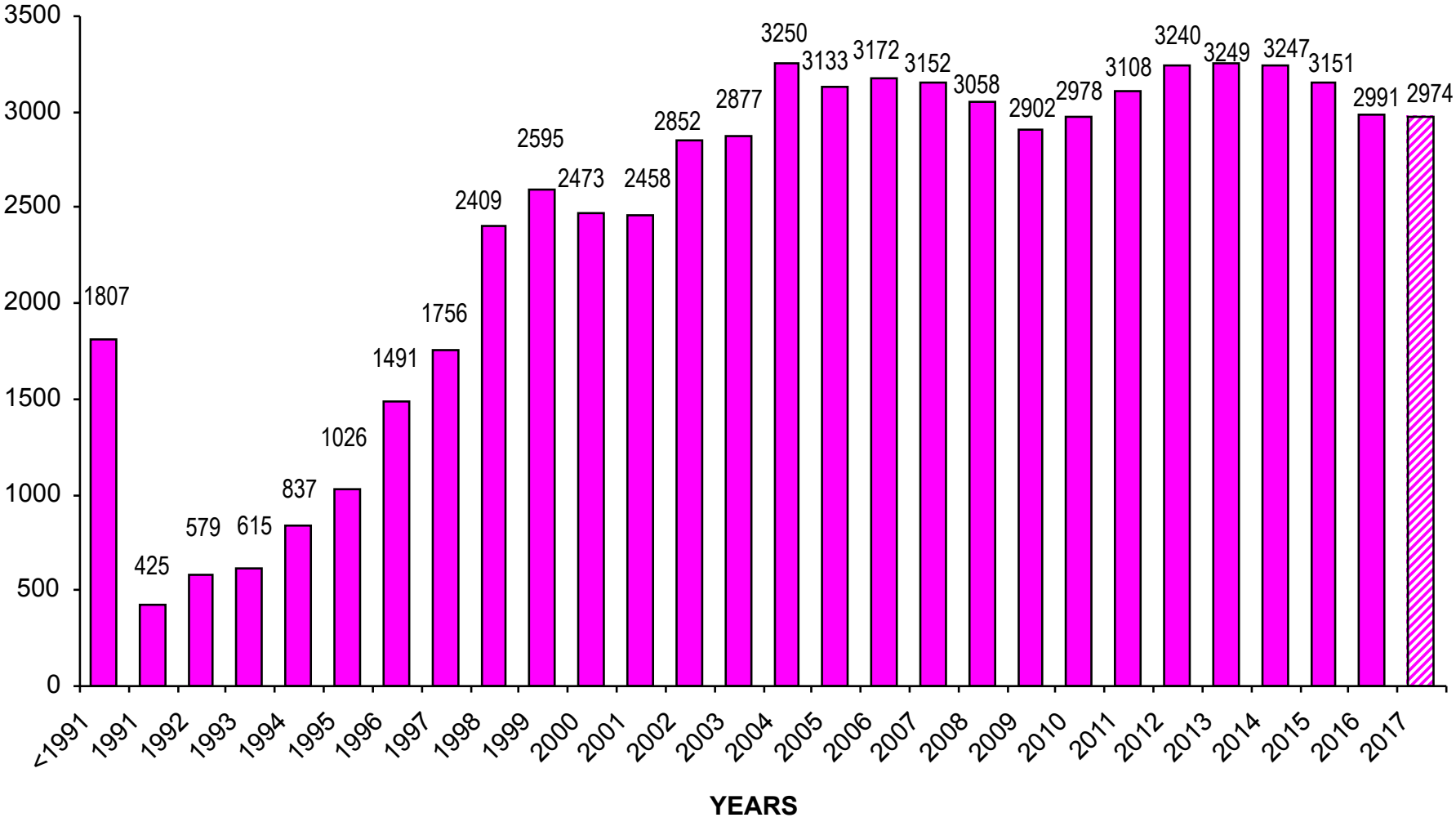
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

TRANSPLANT ACTIVITY

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

Autologous Transplants
(n=67805)



Export date 28/03/2018

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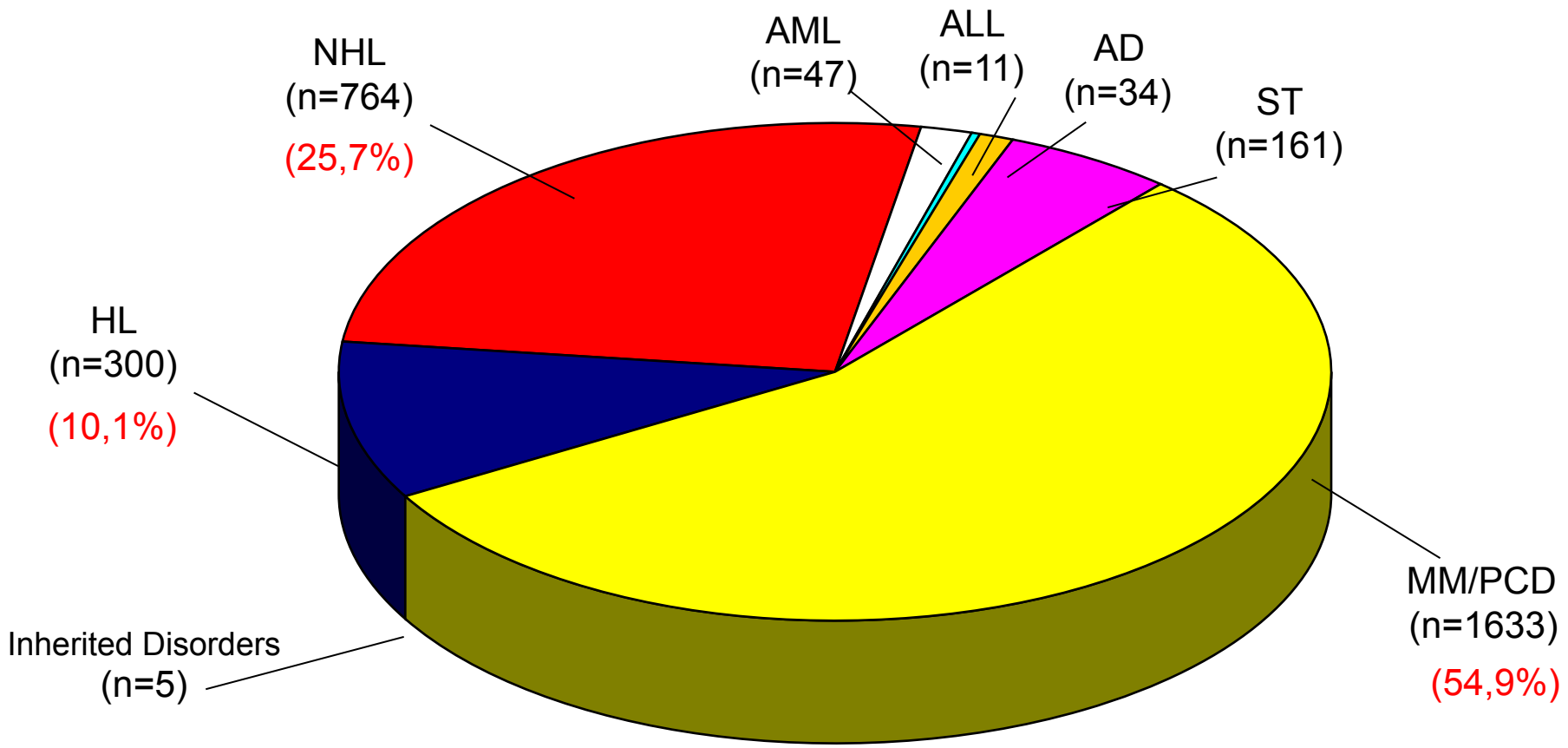
Autologous Tranplants

Indications

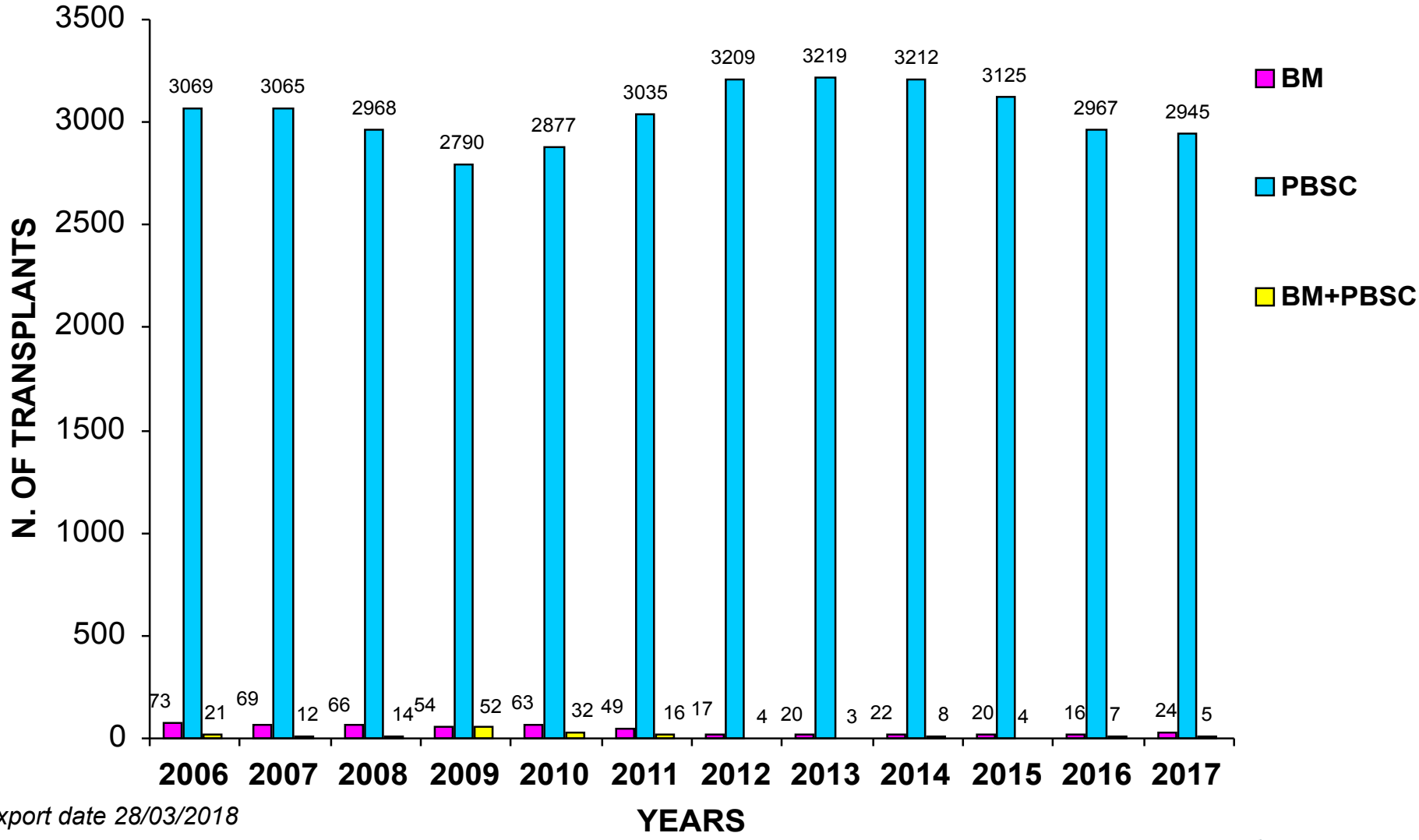
2017



Export date 28/03/2018

Autologous Transplants

Source of HSC



Export date 28/03/2018

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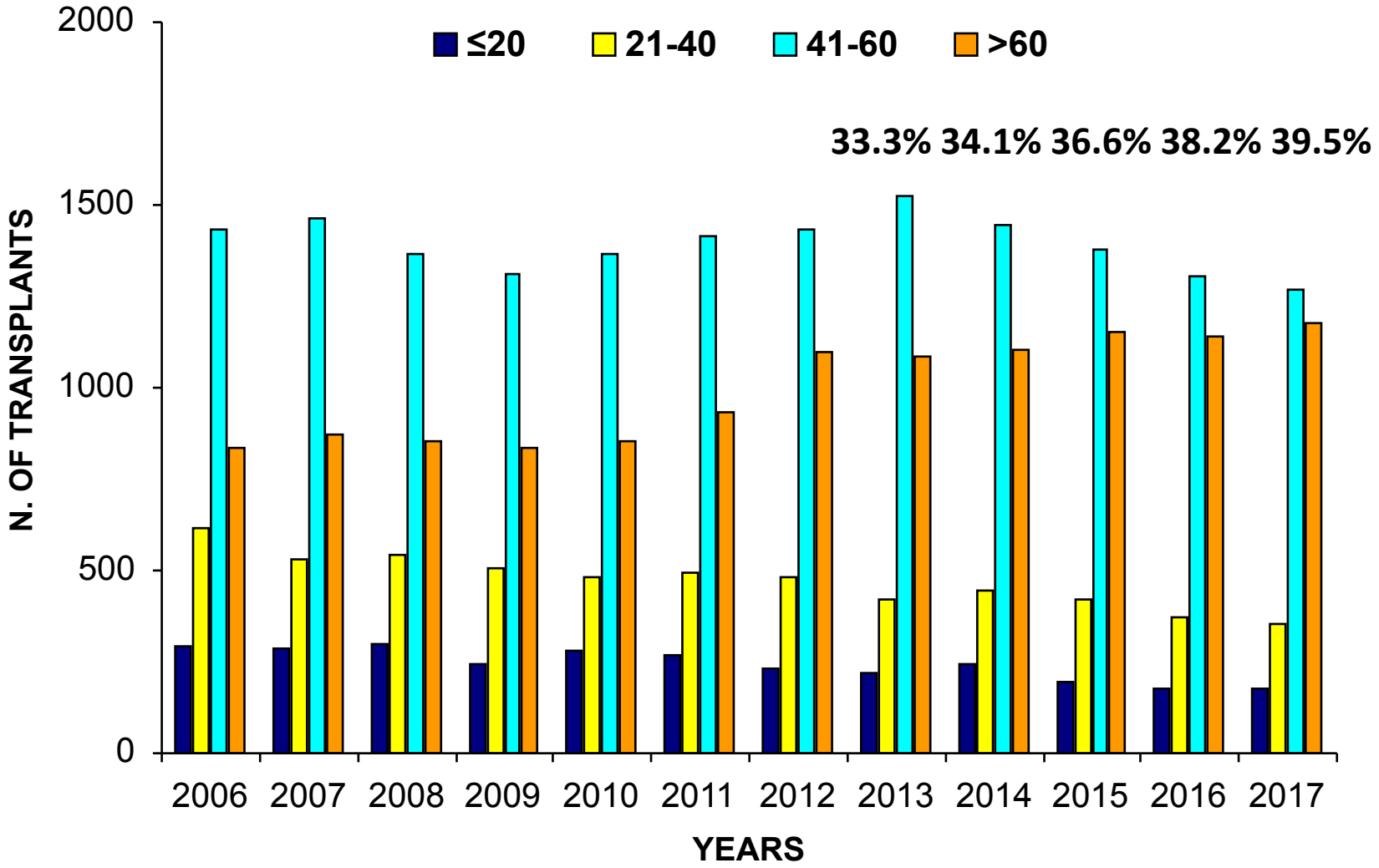
Autologous Transplants

Patients Age at transplantation

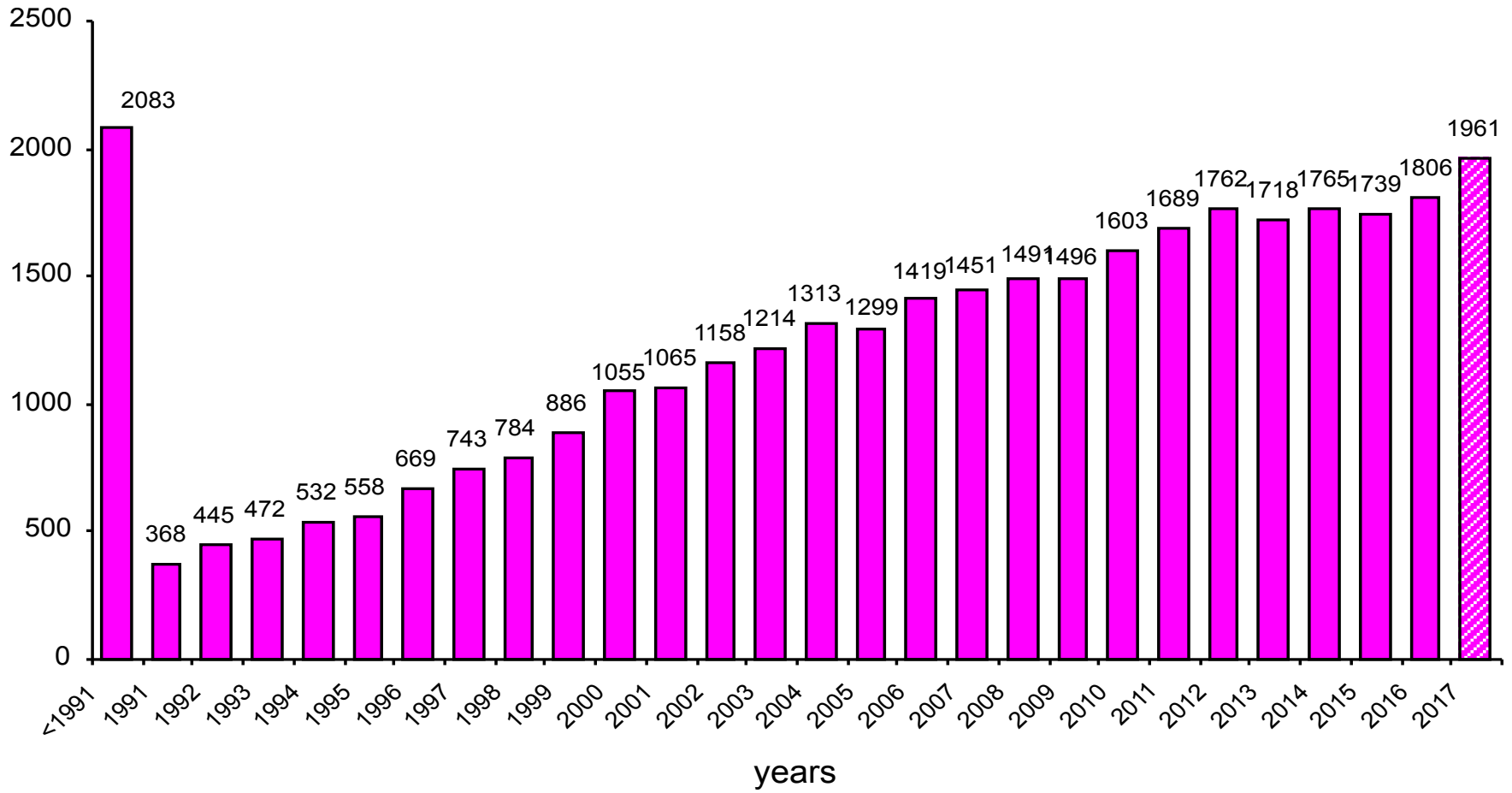


Export date 28/03/2018

GITMO

Allogeneic Transplants

(N=34544)

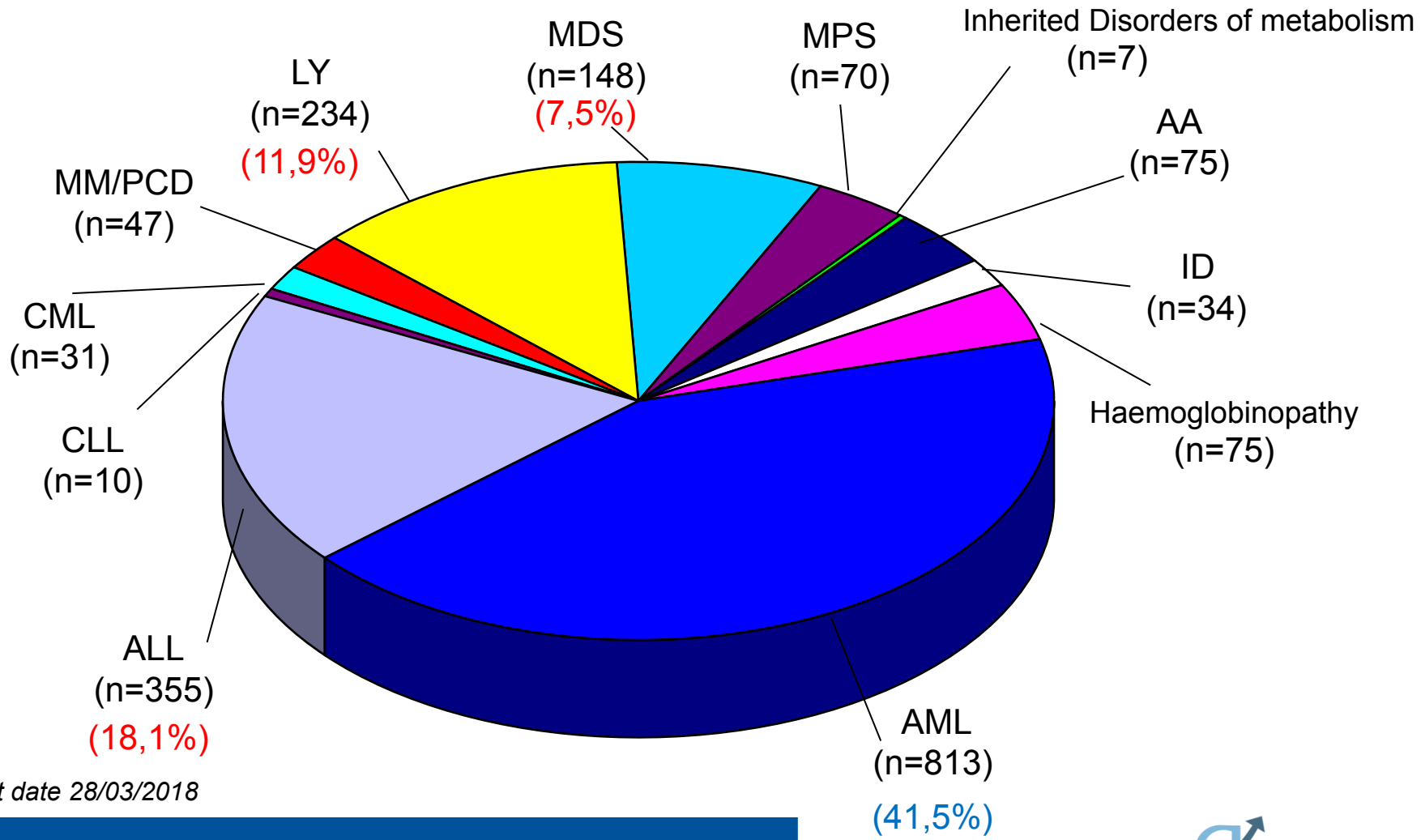


Export date 28/03/2018

GITMO

Allogeneic Transplants

Indications 2017



Export date 28/03/2018

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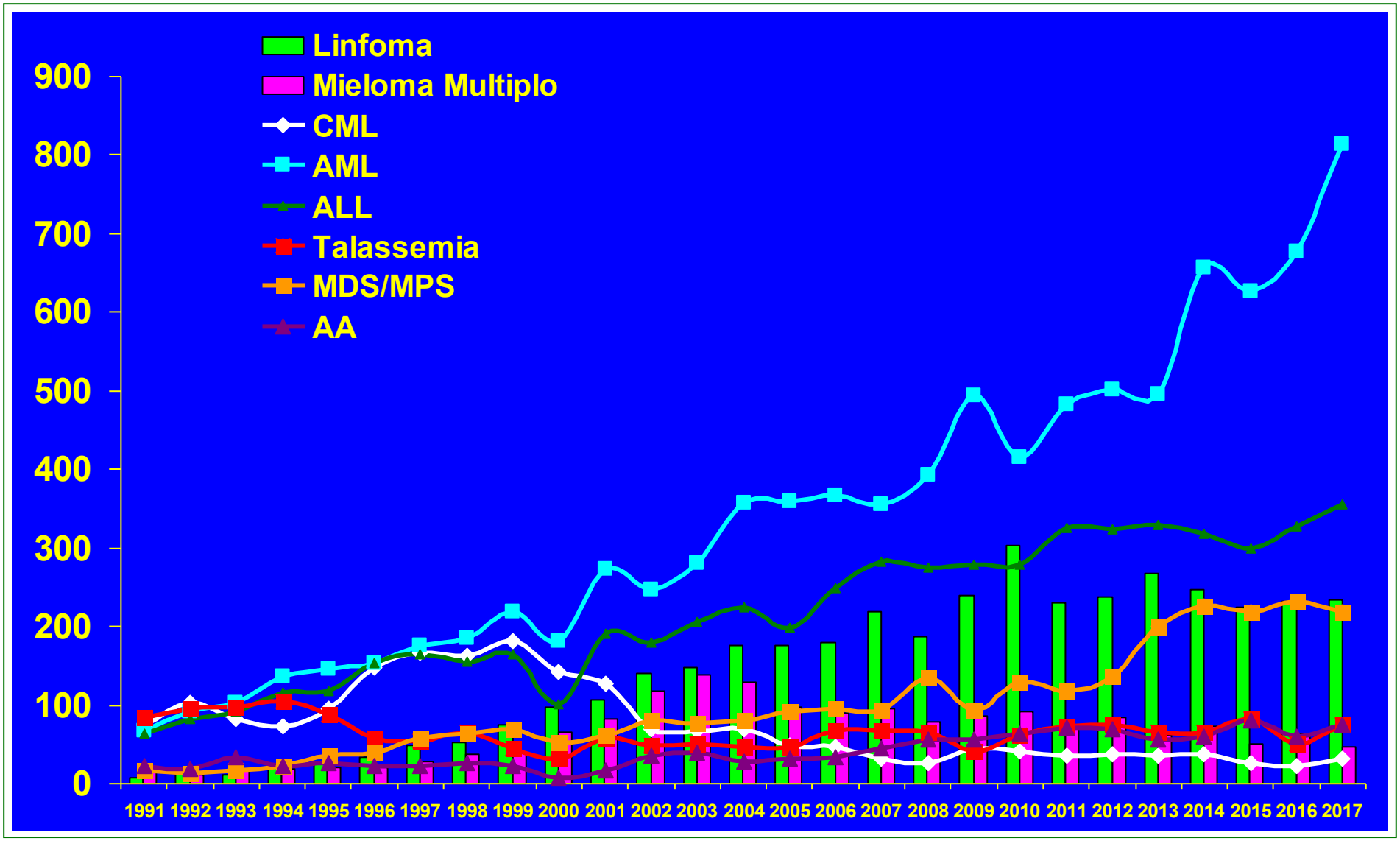
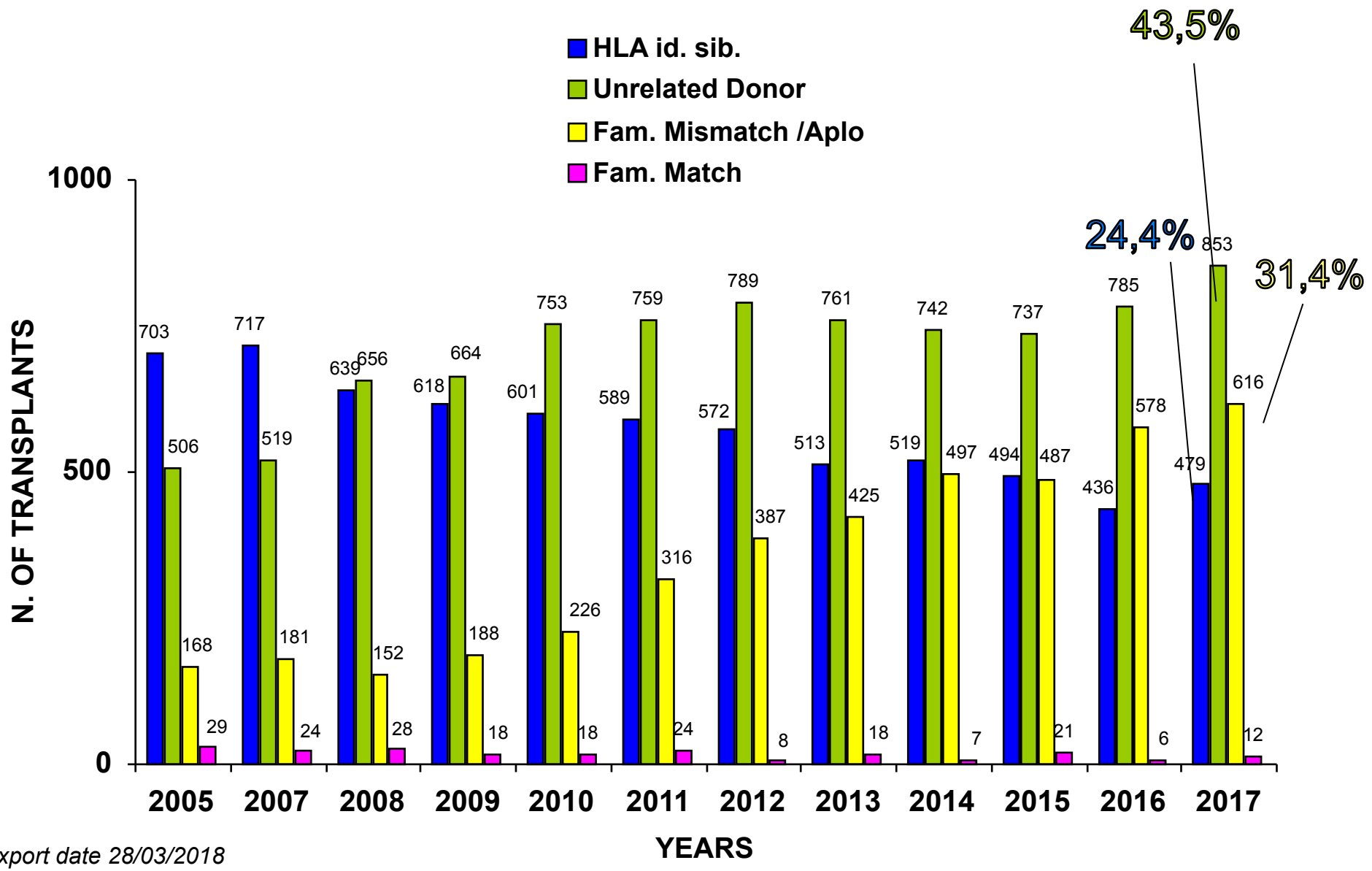
Allogeneic Transplants

Indications over the years



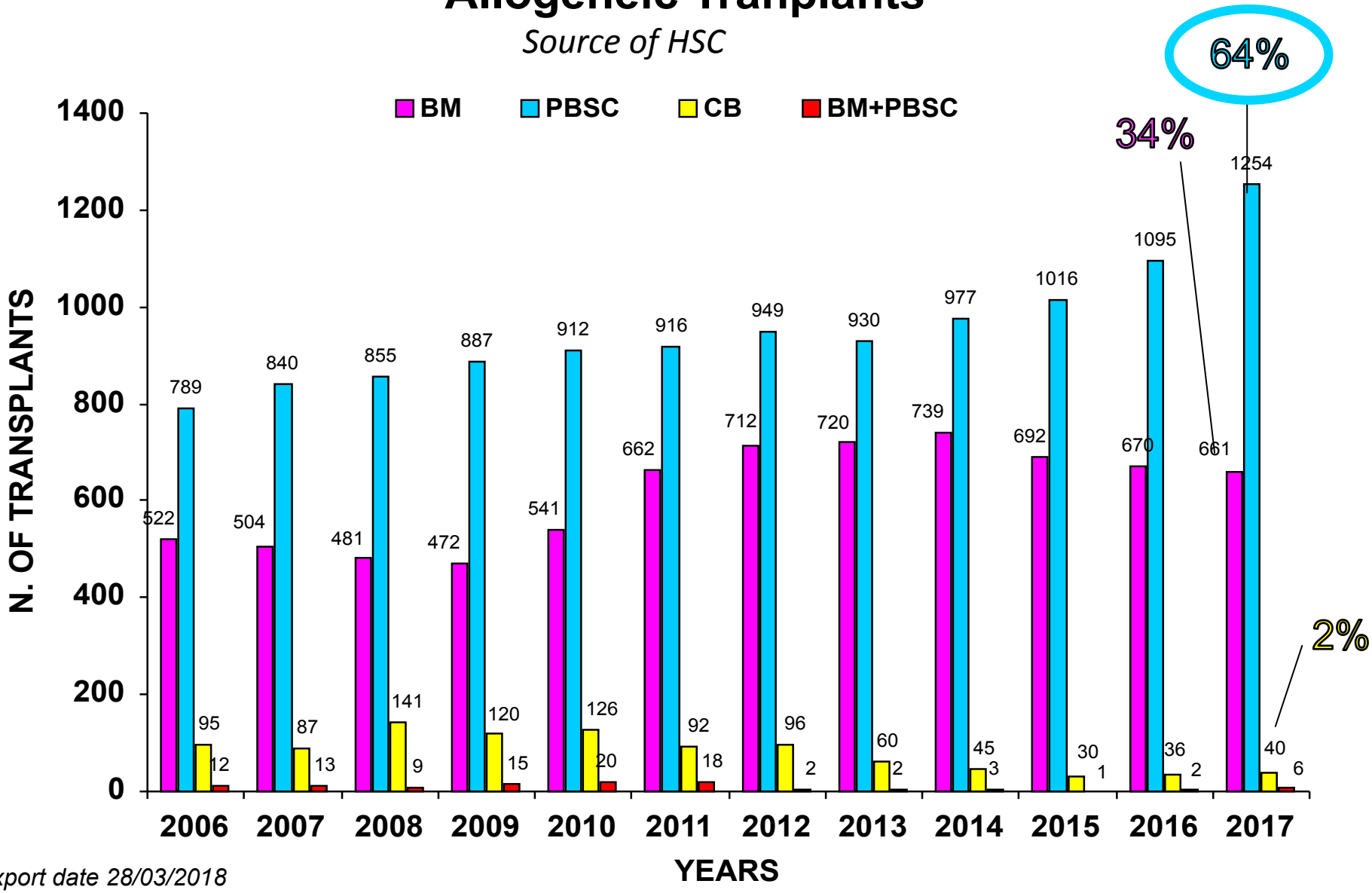
Allogeneic Transplants: *Donor Type*



Export date 28/03/2018

Allogeneic Tranplants

Source of HSC



Export date 28/03/2018

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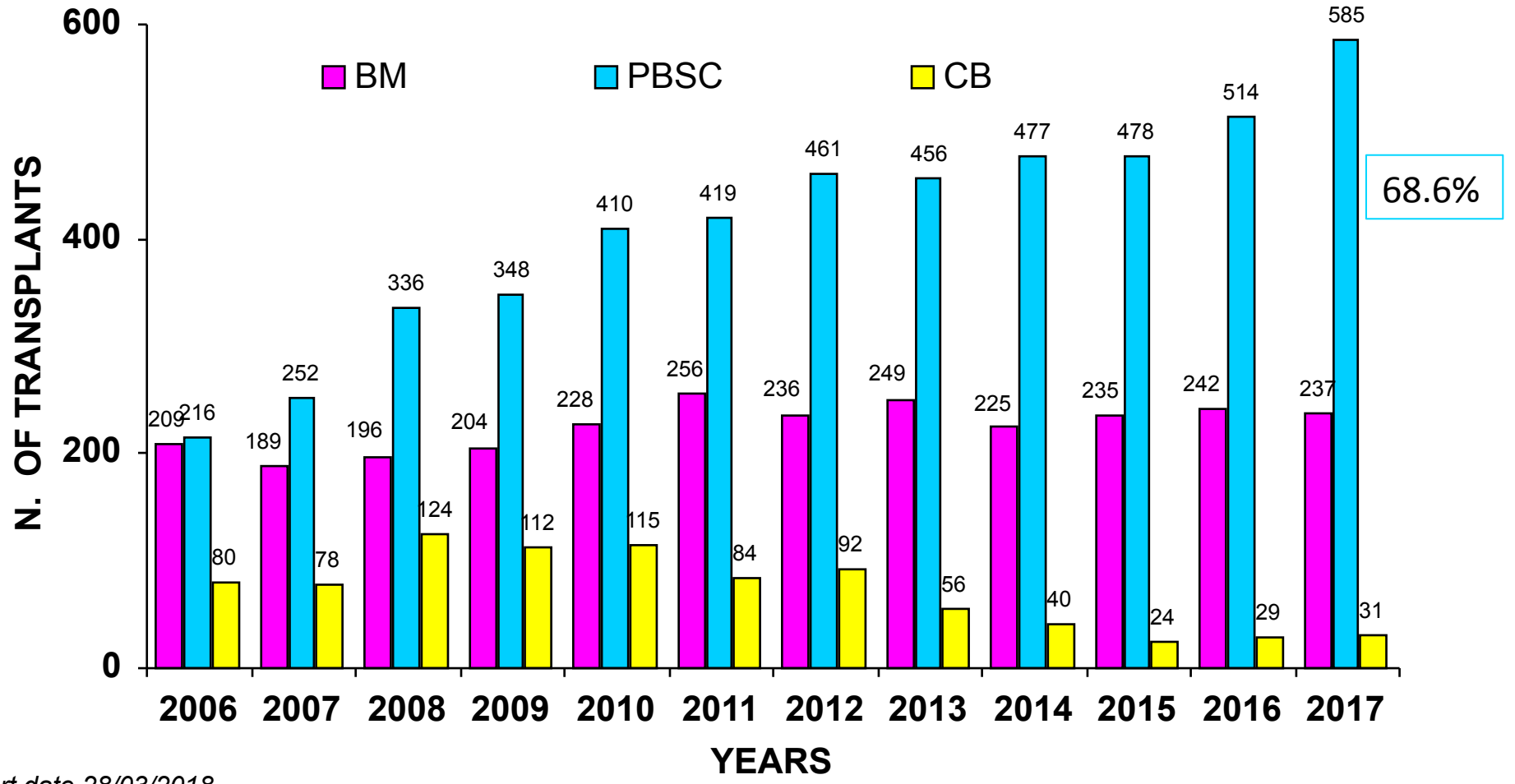
Allogeneic Transplants

Unrelated Donor and Source of HSC



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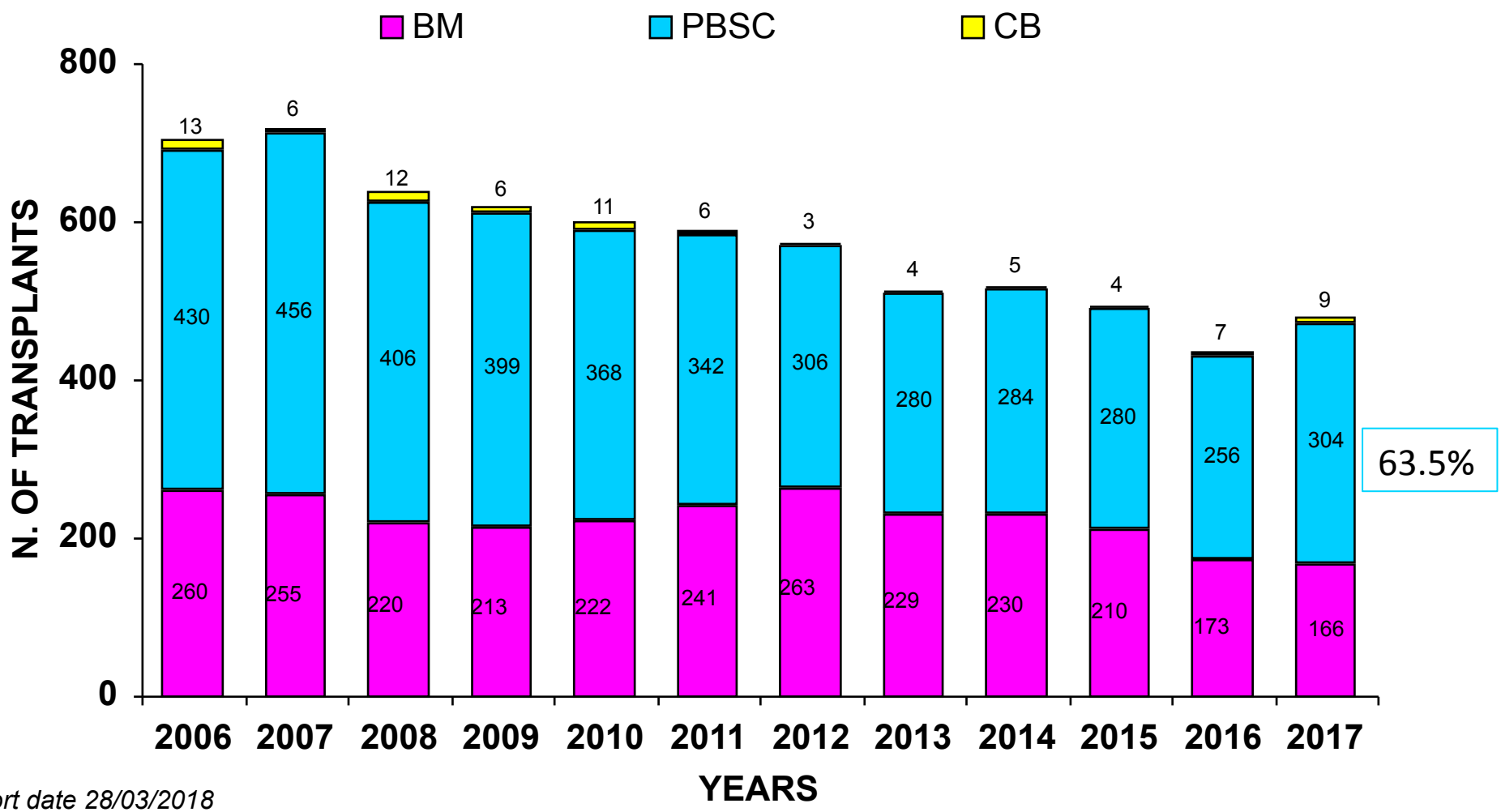
Allogeneic Transplants

HLA id sib donor and Source of HSC



Export date 28/03/2018

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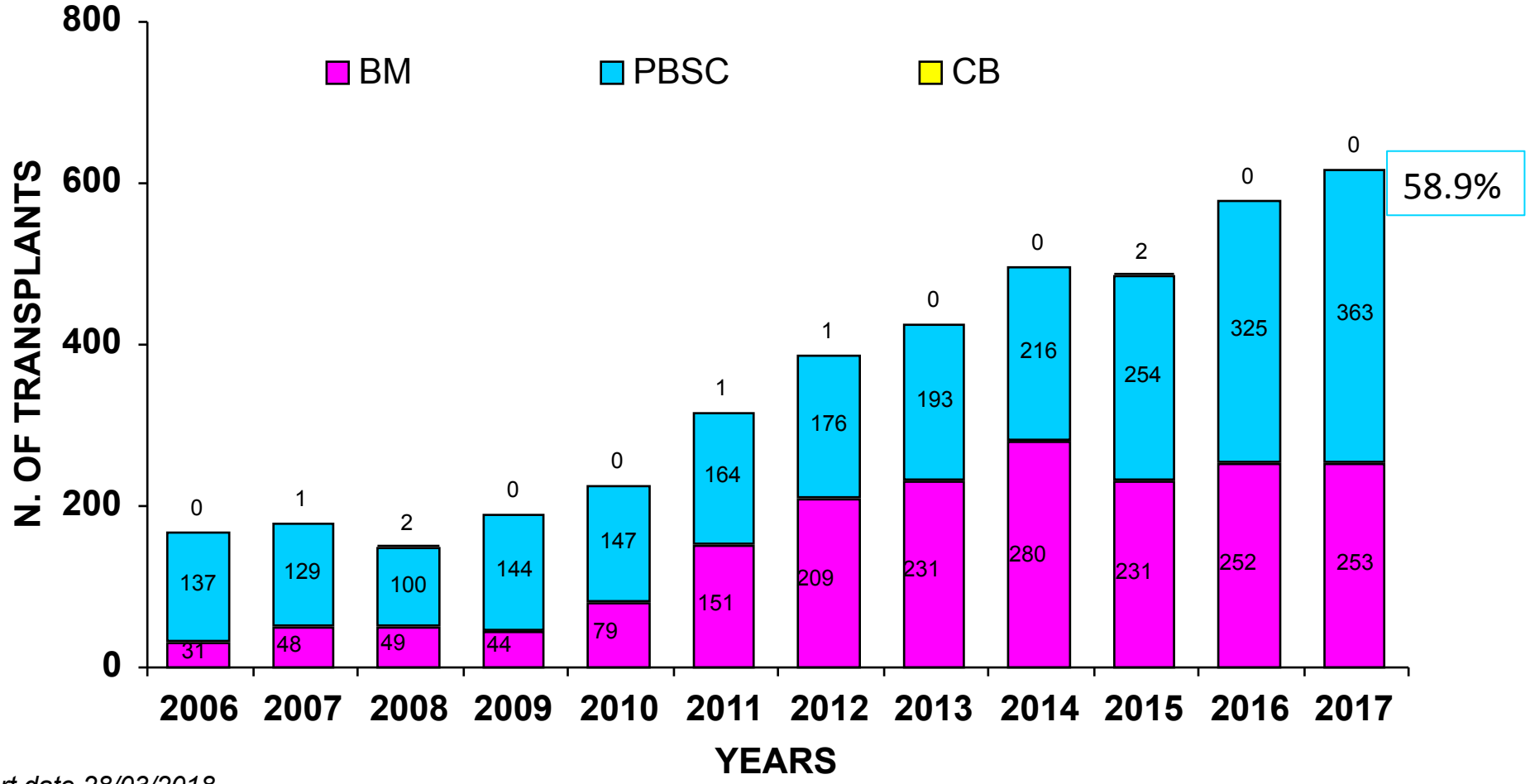
Allogeneic Transplants

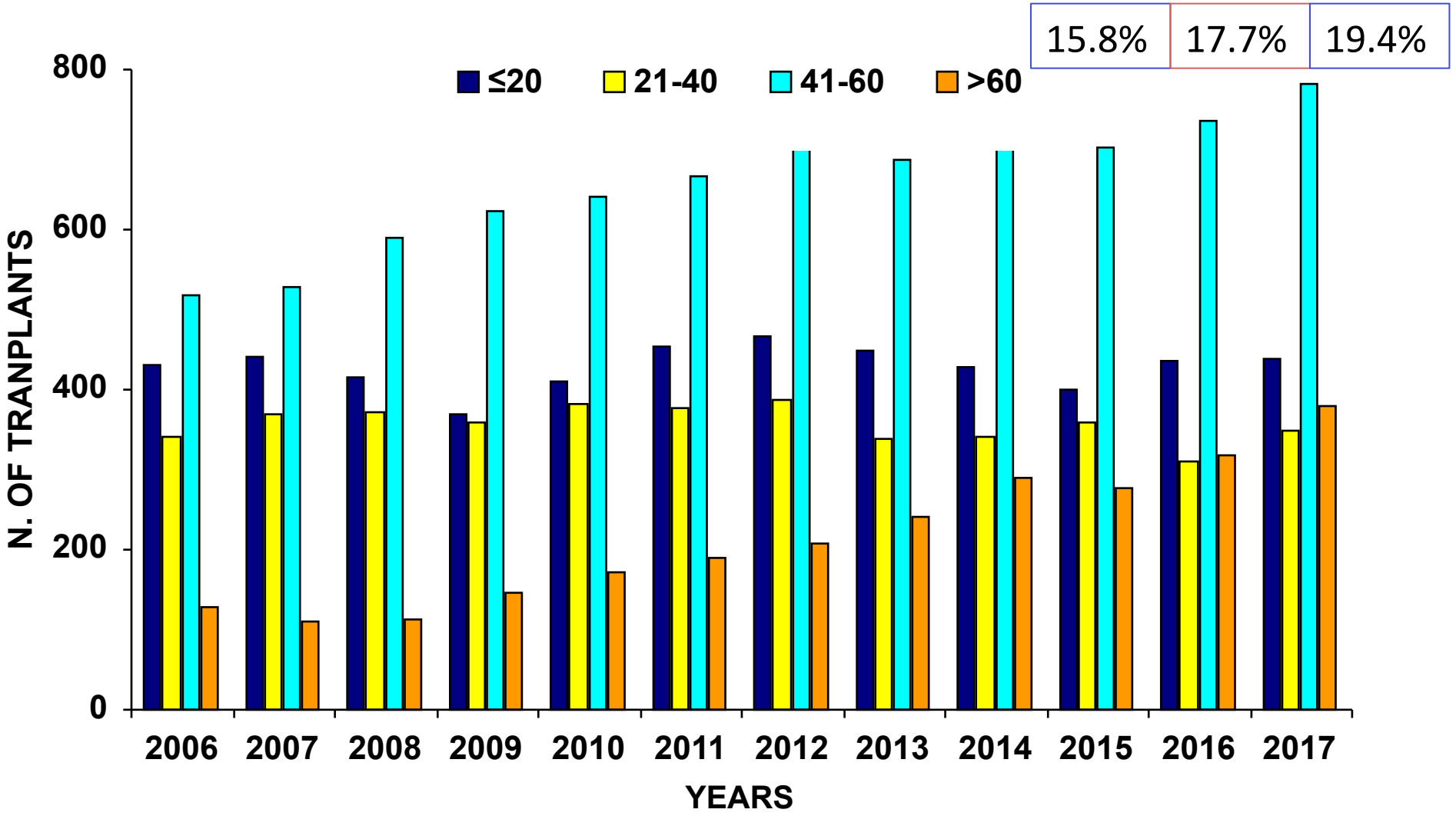
Haplo/Fam Mism Donor and Source of HSC



Export date 28/03/2018

Allogeneic Transplants

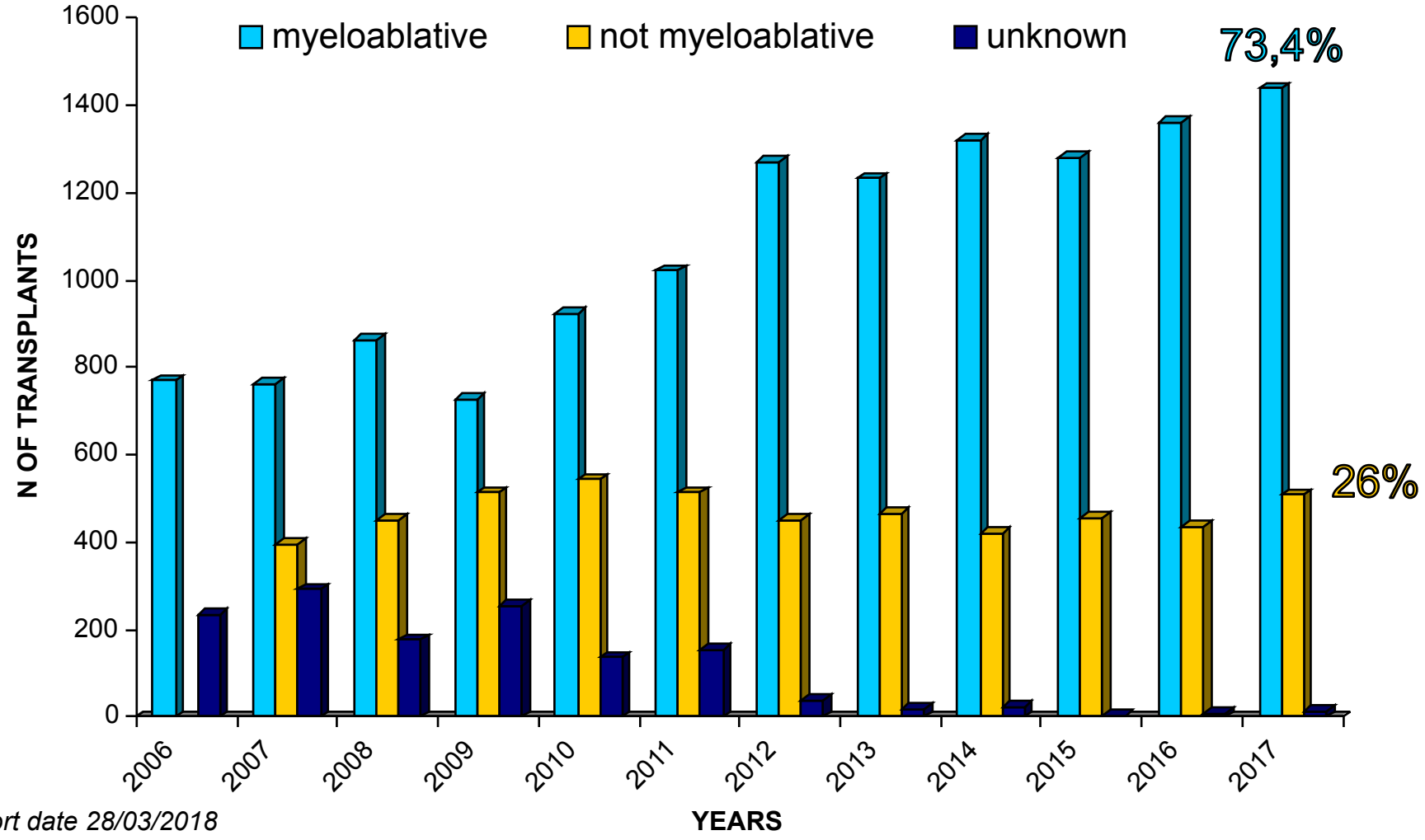
Patient Age at transplantation



Export date 28/03/2018

Allogeneic transplants

Conditioning regimens



Export date 28/03/2018

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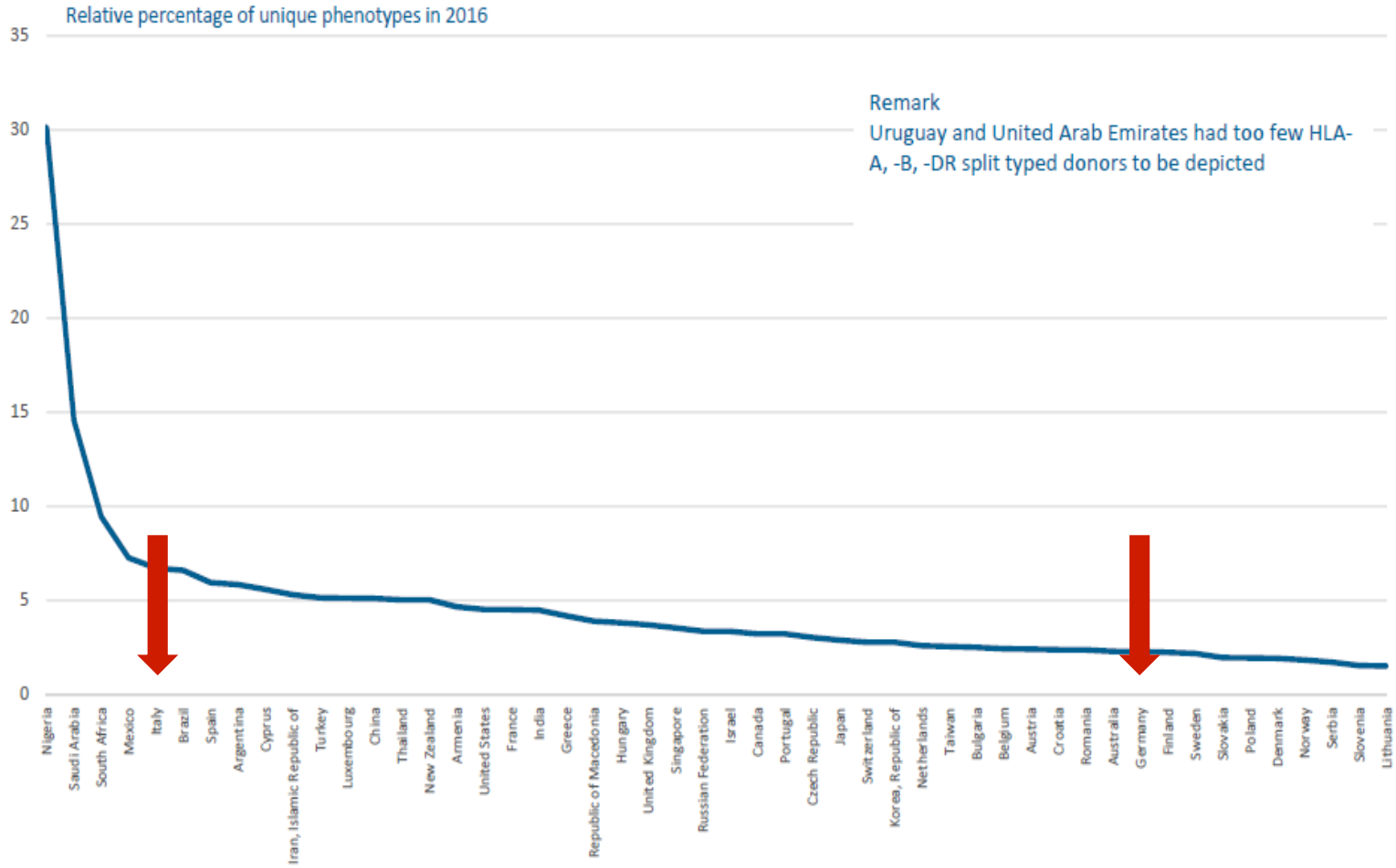
GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

HSC DONATION IN ITALY
ACTIVITY 2017

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

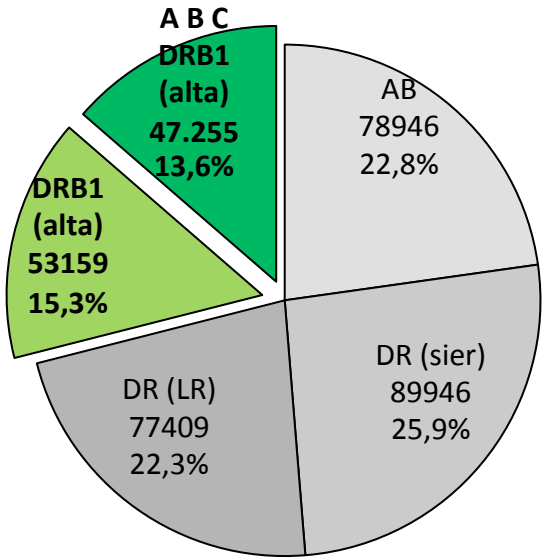
GITMO

RELATIVE PERCENTAGE OF UNIQUE HLA-A, -B, -DR SPLIT PHENOTYPES OF STEM CELL DONORS PER COUNTRY CONTRIBUTED TO THE ENTIRE DATABASE IN BMDW

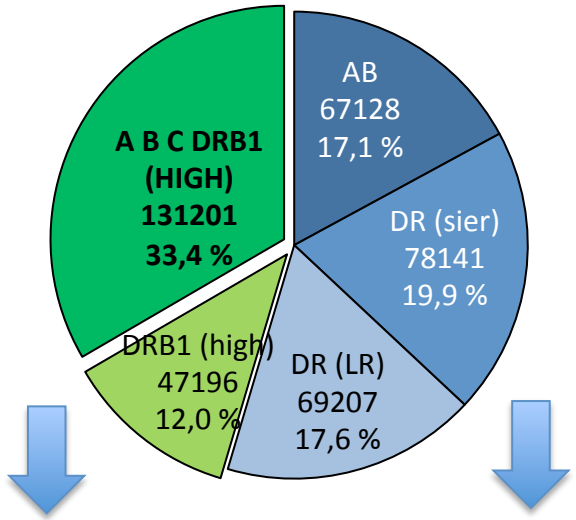


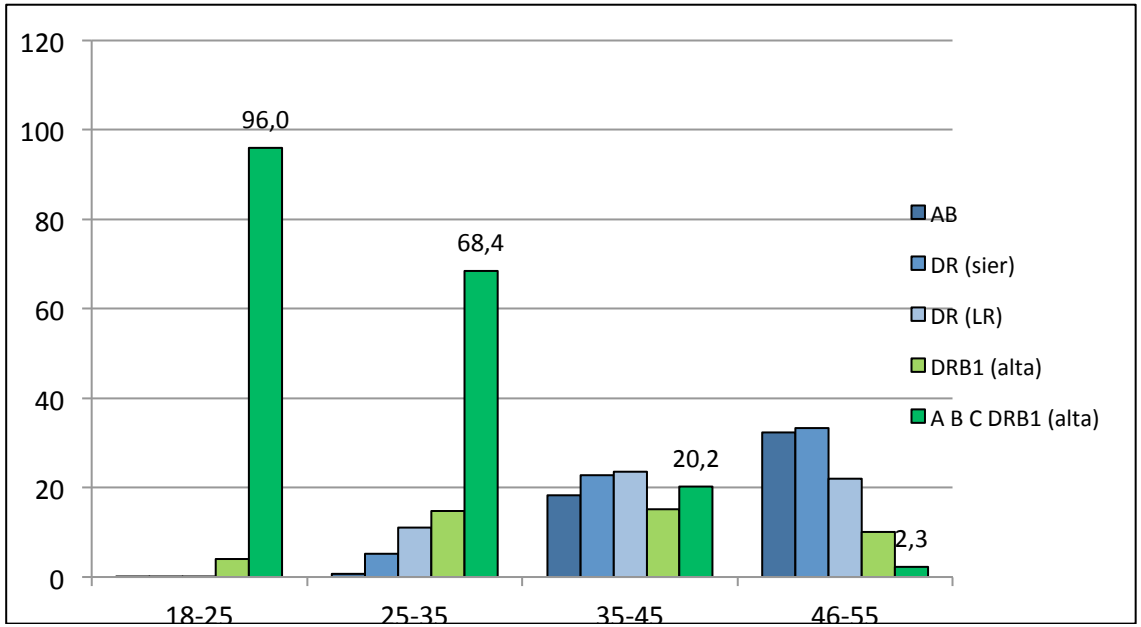
IBMDR: improvement of matching and age distribution

December 2014:
TOTAL ACTIVE DONORS= 346.715

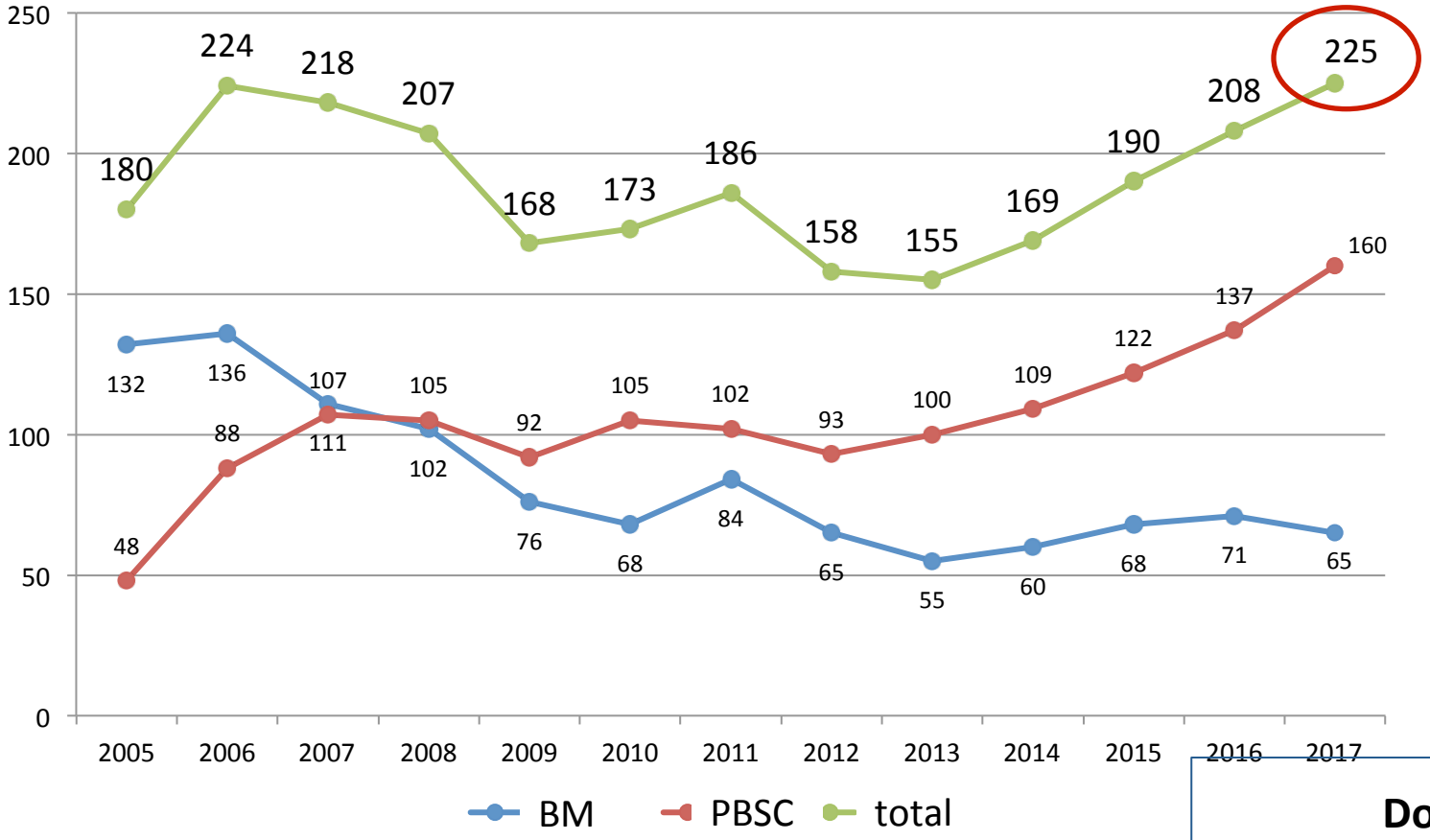


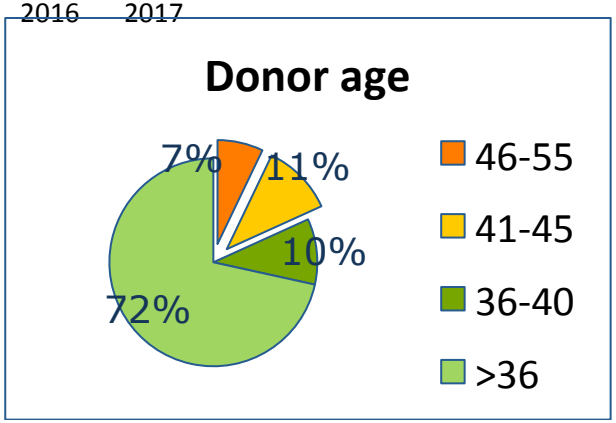
December 2017
TOTAL ACTIVE DONORS = 392.873



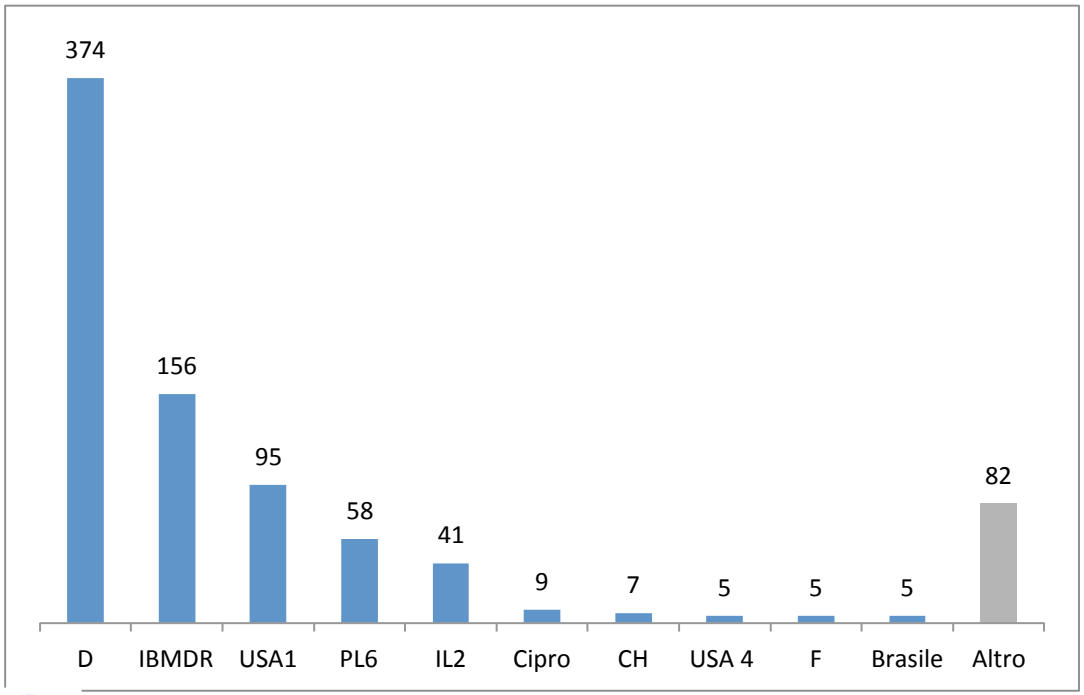


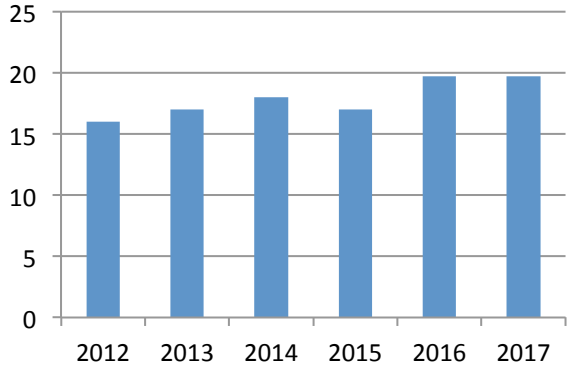
Italian Donations of adult HSC





Adult unrelated donors Registries for Italian patients
(year 2017)



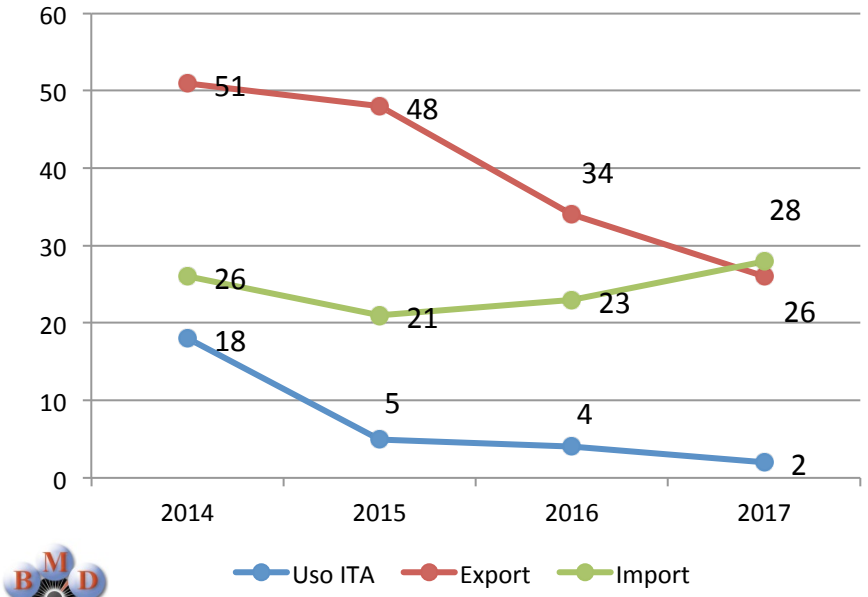


% don. IBMDR

ITALIAN CB BANKS and CBU

CBU Bank	N of exposed CBU dec 31 2017
Bologna ER CBB	4.385
Calabria CBB	842
Campania CBB	1.764
Firenze CBB	2.277
Genova CBB	593
Lazio CBB	1.258
Milano CBB	10.403
Padova CBB	2.407
Pavia CBB	3.792
Pescara CBB	1.522
Pisa CBB	1.013
Puglia CBB	1.248
Sardegna CBB	137
Sciacca CBB	41
Torino CBB	1.854
Treviso CBB	1.084
Unicatt CBB	559
Verona CBB	110
Totale	**35.289**

Import/export of CBUs in Italy



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GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

EDUCATIONAL ACTIVITY

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

GITMO

PLURIANNUAL SCT TRAINING COURSE

Nov 2018: PESCARA

Nov 2019: ANCONA

SEARCH COORDINATOR COURSES

Corso certificativo per Search Coordinator

Milano, San Raffaele 11 aprile 2017

Si certifica che

Il/la Dott. .....

ha partecipato al Corso e conseguito

l'ATTESTATO GITMO/IBMDR di SEARCH COORDINATOR

Il Presidente GITMO

Francesca Bonifazi

Il Direttore Registro IBMDR

Nicoletta Sacchi

GITMO

Registro nazionale Italiano
Donatori Midollo Osseo

I Corso GITMO-IBMDR

per Search Coordinator

11/04/2017

Milano San Raffaele

II Corso GITMO-IBMDR

per Search Coordinator

13/04/2018

Milano San Raffaele

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GRUPPO ITALIANO PER IL TRAPIANTO DI MIDOLLO OSSEO, CELLULE STAMINALI EMOPOIETICHE E TERAPIA CELLULARE

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November 2017

June 2018

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4 SECTIONS (active from April 2016)

EVIDENCE BASED TRANSPLANT
R. Crocchiolo

ALTERNATIVE TRANSPLANT
F.Patriarca (coordinatore)

TRANSPLANT COMPLICATIONS
N. Mordini

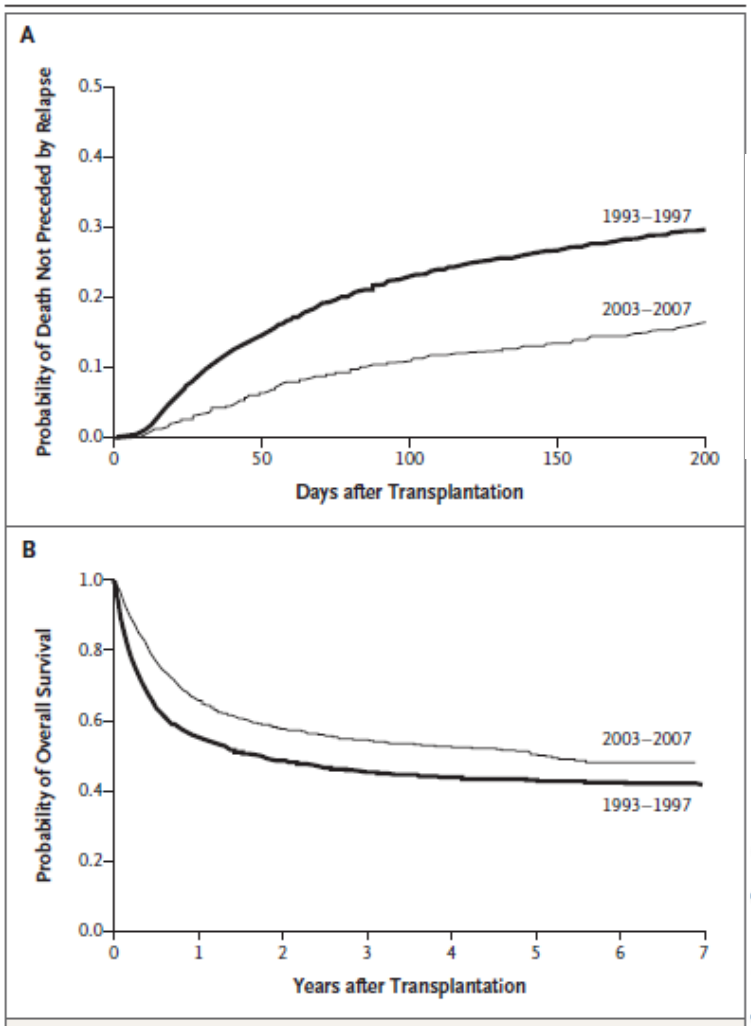
TRASLATIONAL MEDICINE
A. Bondanza

5th section (active from April 2017)

THE NURSES' PERSPECTIVES
G. Gargiulo, S. Botti, L. Orlando

One year activity:
-48 REVIEWED PAPERS/YEAR
-300 followers
-overall >30.000 pagine visited pages

TRANSPLANT OUTCOME IMPROVEMENT



Gooley N Engl J Med 2010

Reduced Mortality after Allogeneic Hematopoietic-Cell Transplantation

Ted A. Gooley, Ph.D., Jason W. Chien, M.D., Steven A. Pergam, M.D., M.P.H., Sangeeta Hingorani, M.D., M.P.H., Mohamed L. Sorror, M.D., Michael Boeckh, M.D., Paul J. Martin, M.D., Brenda M. Sandmaier, M.D., Kieren A. Marr, M.D., Frederick R. Appelbaum, M.D., Rainer Storb, M.D., and George B. McDonald, M.D.

NRM IMPROVEMENT DUE TO

1. ✓ BETTER SUPPORTIVE CARE
2. ✓ REDUCTION OF INTENSITY OF CONDITIONING
3. ✓ AVAILABILITY OF SCORES TO PREDICT NRM
4. ✓ BETTER GVHD PROPHYLAXIS
5. ✓ BETTER MANAGEMENT OF COMPLICATIONS

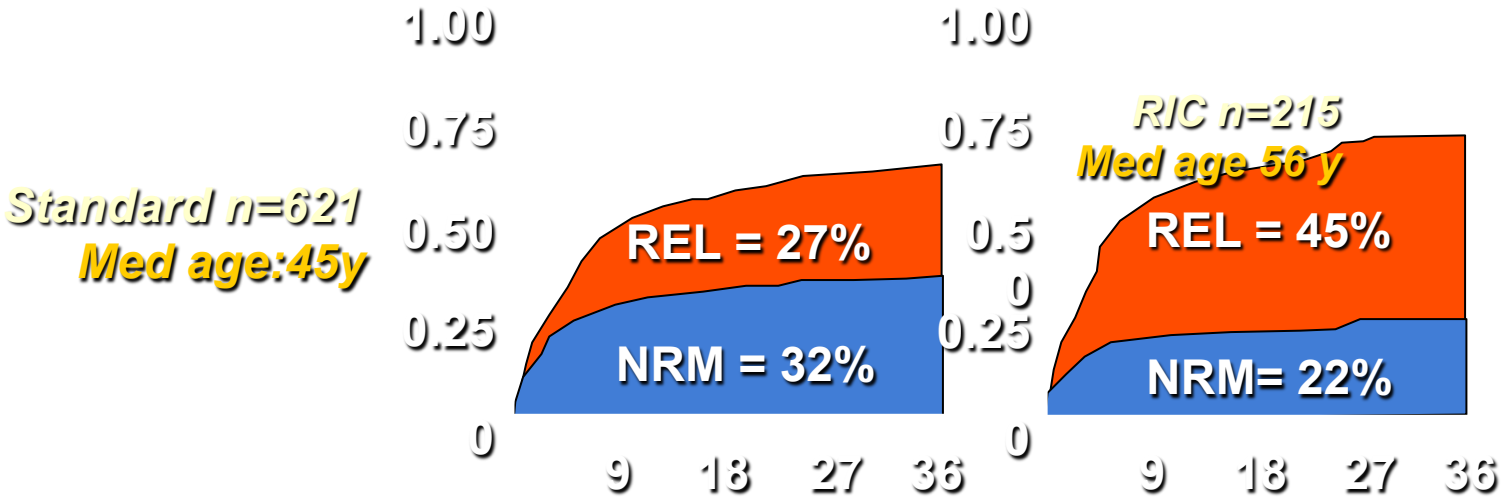
1 IMPROVEMENT OF SUPPORTIVE CARE

Table 2. Comparison of Outcomes, Organ Dysfunction, Infection, and Acute GVHD after Transplantation between the Two Time Periods.*

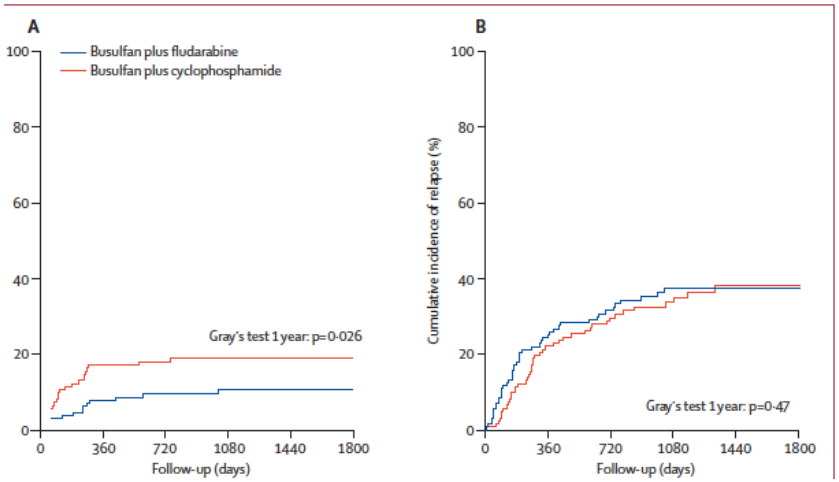
Variable	1993–1997 (N=1418)	2003–2007 (N=1148)	All Patients		Patients Who Underwent Myeloablative Conditioning	
			Adjusted Hazard or Odds Ratio (95% CI)†	P Value	Adjusted Hazard or Odds Ratio (95% CI)†	P Value
Infections through day 100						
CMV infection among CMV-seropositive patients¶	420 (57)	419 (63)	1.02 (0.87–1.20)	0.77	1.04 (0.88–1.23)	0.63
CMV disease among CMV-seropositive patients¶	62 (8)	33 (5)	0.52 (0.32–0.85)	0.009	0.53 (0.31–0.89)	0.02
Gram-negative bacteremia	213 (15)	129 (11)	0.61 (0.48–0.79)	<0.001	0.57 (0.44–0.75)	<0.001
Invasive mold infection	125 (9)	80 (7)	0.49 (0.35–0.71)	<0.001	0.55 (0.38–0.78)	<0.001
Invasive candida infection	99 (7)	10 (1)	0.12 (0.06–0.25)	<0.001	0.15 (0.08–0.29)	<0.001

Gooley N Engl J Med 2010

2 REDUCTION THE INTENSITY OF CONDITIONING



Reduced toxicity regimens



Rambaldi for GITMO 2015

3 SCORES TO PREDICT NRM: EBMT SCORE

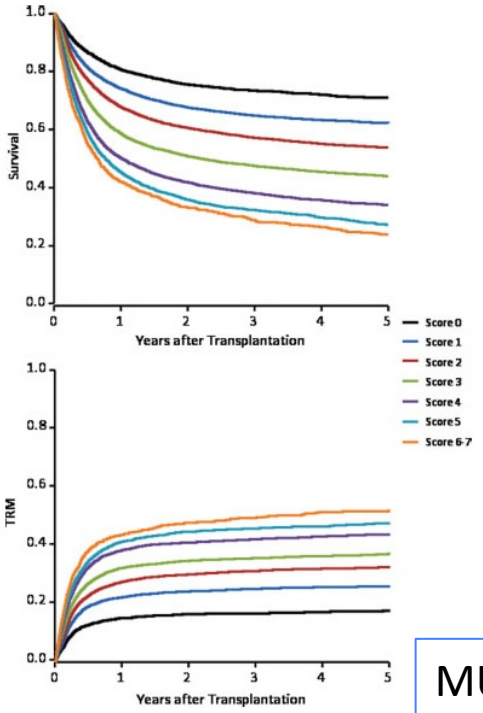
Risk Score for Outcome After Allogeneic Hematopoietic Stem Cell Transplantation

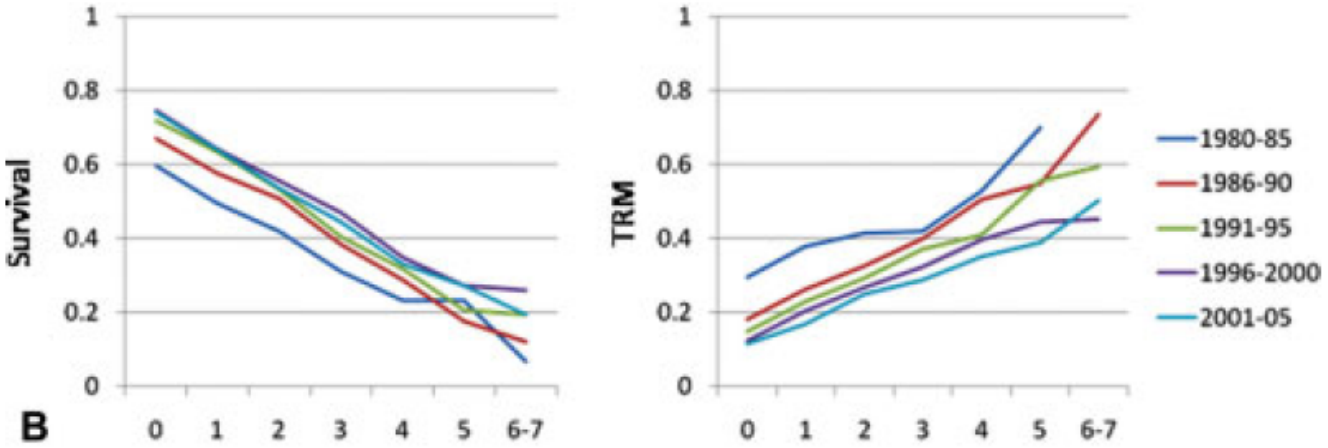
A Retrospective Analysis

Alois Gratwohl, MD[1]; Martin Stern, MD[1]; Ronald Brand[2]; Jane Apperley, MD[3]; Helen Baldomero[1]; Theo de Witte, MD[4]; Giorgio Dini, MD[5]; Vanderson Rocha, MD[6]; Jakob Passweg, MD[7]; Anna Sureda, MD[8]; André Tichelli, MD[9]; and Dietger Niederwieser, MD[10] for the European Group for Blood and Marrow Transplantation and the European Leukemia Net

BACKGROUND: It was investigated whether the European Group for Blood and Marrow Transplantation risk score, previously established for chronic myeloid leukemia, could be used to predict outcome after allogeneic hematopoietic stem cell transplantation (HSCT) for hematological disease in general. **METHODS:** Age of patient, disease stage, time interval from diagnosis to transplant, donor type, and donor-recipient sex combination were used to establish a score from 0 to 7 points. Its validity was tested in 56,505 patients, 33,113 (58%) male, 23,392 female, median age 33 years (range, 0.5-77 years), with an allogeneic HSCT for a hematological disorder between 1980 and 2005. **RESULTS:** Survival probability at 5 years decreased from 71% (95% confidence interval [CI], 69%-73%) for risk score 0 for the whole cohort (75%, 95% CI, 72%-78% for the most recent time cohort) to 24% (95% CI, 21%-27% for risk score 6 and 7; 25%, 95% CI, 22%-29% most recent cohort). Transplant-related mortality increased from 15% (95% CI, 14%-17%) for risk score 0 (11%, 95% CI, 9%-13%, most recent cohort) to 47% with risk score 6 and 7 (95% CI, 44%-50%) for the whole cohort (45%, 95% CI, 42%-48%, most recent cohort). The risk score was predictive in all

***Cancer* 2009 Oct 15;115(20):4715-26**





MUD VS SIB
Fd/Mr vs all others
Age<20 20-40 >40
Dis phase
Interval dg-tx

3 SCORES TO PREDICT NRM: SORROR SCORE

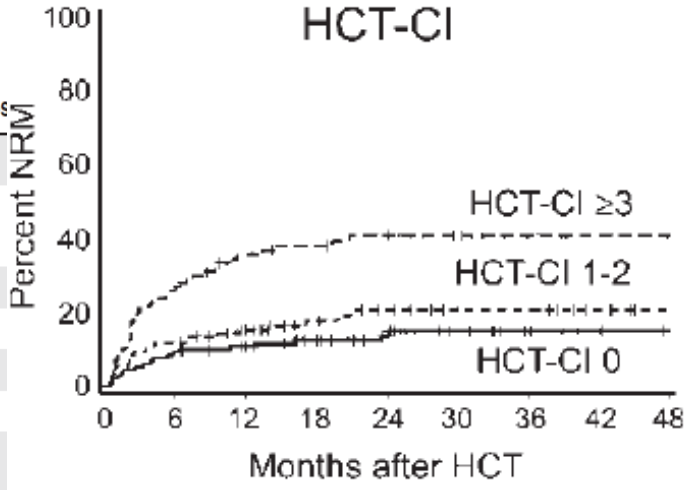
blood 2005;106: 2912-2919

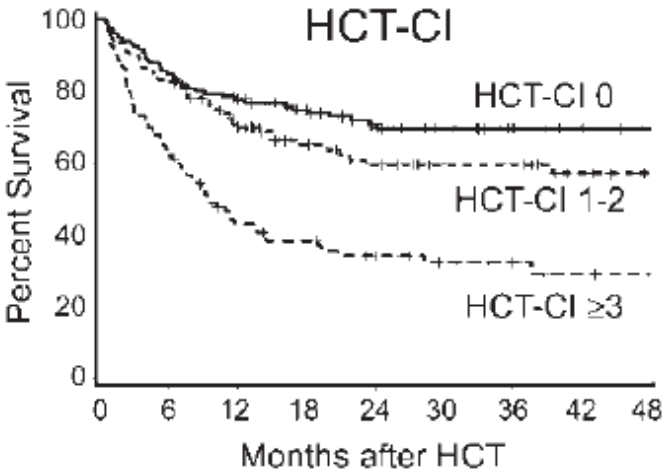
Hematopoietic cell transplantation (HCT)–specific comorbidity index: a new tool for risk assessment before allogeneic HCT

Mohamed Sorror, Michael Maris, Rainer Storb, Frederic Baron, Brenda Sandmaier, David Maloney, Barry Storer

Retrospective study
years 1997-2003. Patients 798

Comorbidity	Definitions of comorbidities included in the new HCT-CI	HCT-CI weighted scores
Arrhythmia	Atrial fibrillation or flutter, sick sinus syndrome, or ventricular arrhythmias	1
Cardiac‡	Coronary artery disease,§ congestive heart failure, myocardial infarction, or EF ≤ 50%	1
Inflammatory bowel disease	Crohn disease or ulcerative colitis	1
Diabetes	Requiring treatment with insulin or oral hypoglycemics but not diet alone	1
Cerebrovascular disease	Transient ischemic attack or cerebrovascular accident	1
Psychiatric disturbance†	Depression or anxiety requiring psychiatric consult or treatment	1
Hepatic, mild‡	Chronic hepatitis, bilirubin > ULN to 1.5 × ULN, or AST/ALT > ULN to 2.5 × ULN	1
Obesity†	Patients with a body mass index > 35 kg/m^2	1
Infection†	Requiring continuation of antimicrobial treatment after day 0	1
Rheumatologic	SLE, RA, polymyositis, mixed CTD, or polymyalgia rheumatica	2
Peptic ulcer	Requiring treatment	2
Moderate/severe renal‡	Serum creatinine > 2 mg/dL, on dialysis, or prior renal transplantation	2
Moderate pulmonary‡	DLco and/or FEV_1 66%-80% or dyspnea on slight activity	2
Prior solid tumor‡	Treated at any time point in the patient's past history, excluding nonmelanoma skin cancer	3
Heart valve disease	Except mitral valve prolapse	3
Severe pulmonary‡	DLco and/or FEV_1 ≤ 65% or dyspnea at rest or requiring oxygen	3
Moderate/severe hepatic‡	Liver cirrhosis, bilirubin > 1.5 × ULN, or AST/ALT > 2.5 × ULN	3





3 SCORES TO PREDICT NRM: ALWP SCORE

VOLUME 33 · NUMBER 28 · OCTOBER 1 2015

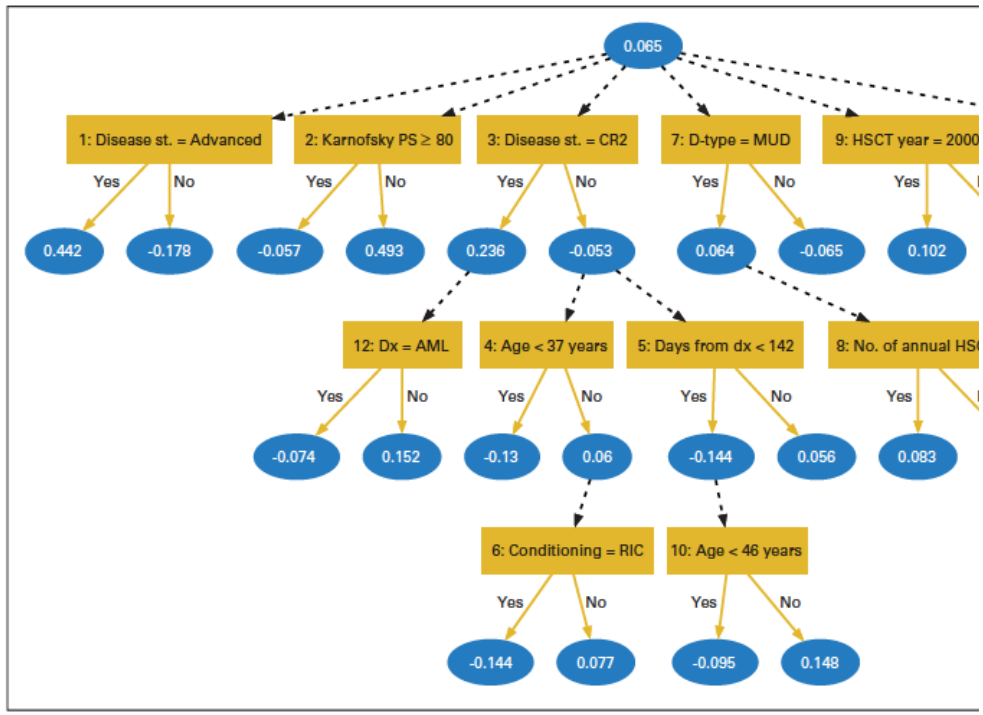
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Prediction of Allogeneic Hematopoietic Stem-Cell Transplantation Mortality 100 Days After Transplantation Using a Machine Learning Algorithm: A European Group for Blood and Marrow Transplantation Acute Leukemia Working Party Retrospective Data Mining Study

Roni Shouval, Myriam Labopin, Ori Bondi, Hila Mishan-Shamay, Avichai Shimoni, Fabio Ciceri, Jordi Esteve, Sebastian Giebel, Norbert C. Gorin, Christoph Schmid, Emmanuelle Polge, Mahmoud Aljurf, Nicolaus Kroger, Charles Craddock, Andrea Bacigalupo, Jan J. Cornelissen, Frederic Baron, Ron Unger, Arnon Nagler, and Mohamad Mohty

Predicting Allo-HSCT Outcomes With a Machine Learning Approach



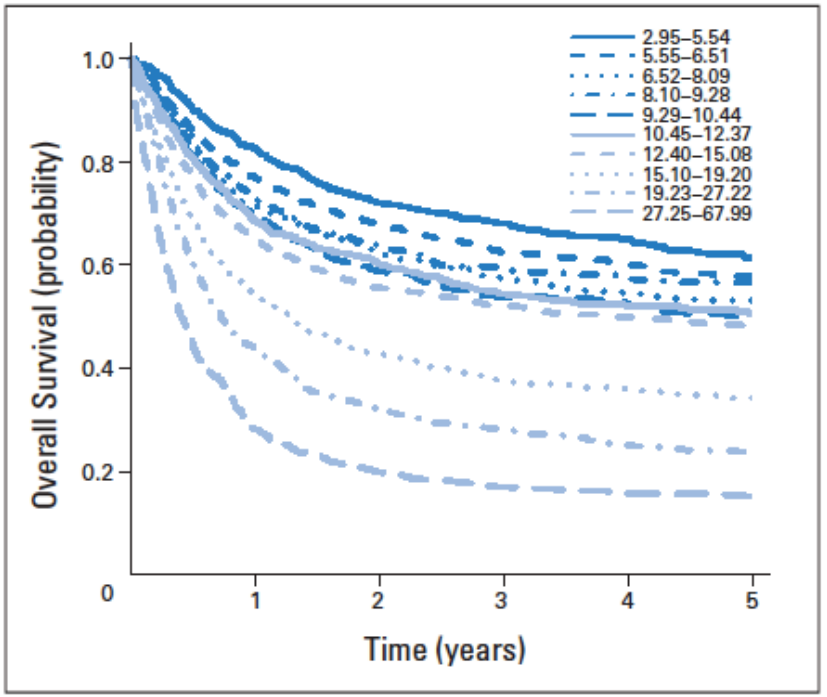
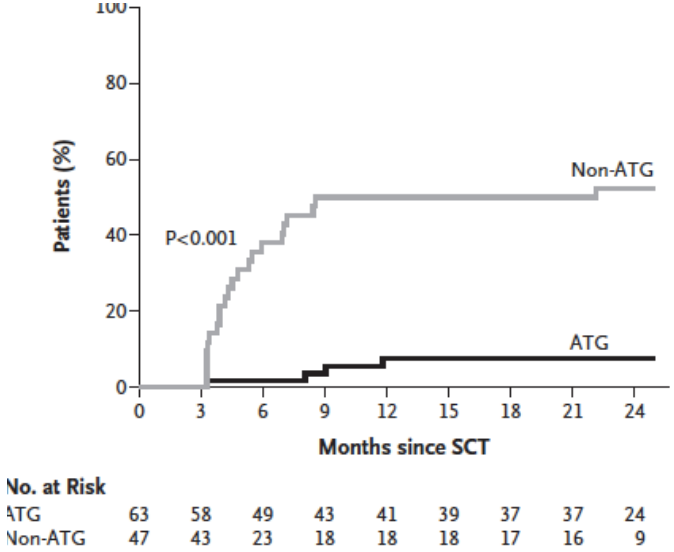


Fig 3. Kaplan-Meier curves of overall survival stratified by the categorized

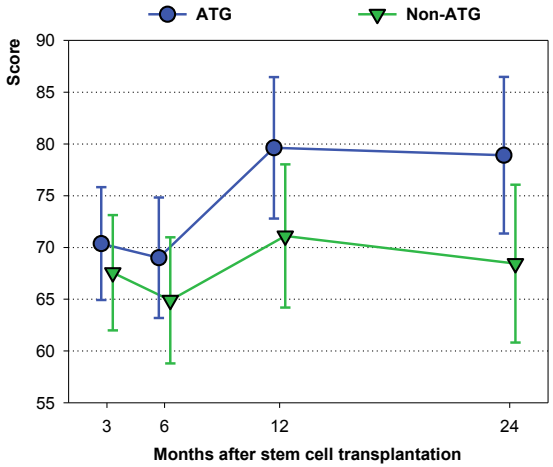
4 IMPROVEMENT OF GVHD PROPHYLAXIS

EXTENSIVE cGVHD



Kröger N et al. N Engl J Med 2016; 374:43-53

GLOBAL HEALTH STATUS
(QLQ-30)



2.8±3.9

10.5±5.3

Bonifazi F et al submitted

GITMO REGISTRY DATA ON ITALIAN ACTIVITY 2012-2016

	2012	2013	2014	2015	2016
N of transpl	1763	1717	1765	1739	1805
HLA id sibl	32.7	30.7	29.5	29.4	24.1
VUD	39.6	41.1	39.8	41.0	41.9
Mism rel (haplo)	22.1	24.7	28.2	27.9	32.0
CBT	5.4	3.5	2.5	1.7	2.9
PBSC	53.8	54.2	55.3	58.4	60.8
ATG yes	49.3	50.5	47.6	50.0	53.1
Edx yes	15.6	17.9	21.1	22.6	23.7
aGVHD gr 2-4	23.4	23.3	21.5	20.7	19.5
aGVHD gr 3-4	9.3	7.5	7.2	8.7	5.7

Thanks to Dr. E. Oldani for preliminary data

5 IMPROVEMENT OF COMPLICATIONS' MANAGEMENT: VOD/SOS

GITMO THREE STEPS PROJECT

- **14 members of GITMO Transplant programs**
- **Physicians and nurses**
- **Clinical methodology team HEADED BY GIOVANNI POMPONIO**
- **Started on 2016, April**
- **Completion: end of 2018**

Alice Bertaina
Francesca Bonifazi
Stefano Botti
Alessandro Busca
Angelo Maria Carella
Raffaella Cerretti
Anna Paola Iori
Giampaolo Gargiulo
Anna Grassi
Francesca Gualandi
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Sarah Marktel
Giuseppe Milone
Arcangelo Prete
Stella Santarone
Simona Sica
Elena Vassallo
Marco Zecca

Giovanni Pomponio
Laura Postacchini
Alessia Angeletti
Diletta Olivari
Giulia Rossetti

Background

- VOD/SOS IS A RARE BUT SEVERE HSCT COMPLICATION
- CONTROLLED CLINICAL TRIALS ARE SCARSE AND CLINICAL PRATICE IS CHARACTERISED BY HIGH DEGREE OF VARIABILITY

Aim

Reaching a sufficient consensus level for recommendations which will define the GITMO **'good clinical practice'**

Steering commitee

Expert panel

DEFINITION OF SCENARIA (population, intervention, outcome)

Steering commitee

Expert panel

not relevant scenaria,

formulation of 'focused questions'

Relevant Focused Questions
Population, Intervention(s), Outcome(s)

Steering commitee

Librarian

Expert panel
+metodologist

evidence tables, grey literature

Draft of recommendations

Tick in the box which best corresponds to your assessment, in terms of benefit versus disadvantages

In patients with pressure ulcers without evidence of infection, the application of an antiseptic foam is recommended

	1	2	0	2	1
Balance between desirable and undesirable consequences of the intervention	Desirable clearly outweighs undesirable	Desirable probably outweighs undesirable	Trade-offs equally balanced or uncertain	Undesirable probably outweighs desirable	Undesirable clearly outweighs desirable
GRADE score	**STRONG:** "definitely do it"	**WEAK:** "probably do it"	**No specific recommendation**	**WEAK:** "probably don't do it"	**STRONG:** "definitely don't do it"

CRITICAL outcomes

Carica microbica – Colony Count, Microbial ……..(continues)

IMPORTANT, NOT CRITICAL

Cellulite – Cellulitis, …… (continues)

EVIDENCE TABLES (continues below)

Ref.	Condition	Population	Design	Interventions	Outcomes	Results	Comments	Level of evidence

List of preliminary recommendations

Expert panel

Plenary discussion about recommendations

2018 June 22nd

Final list of recommendations
Grading (Strong, Weak)

Steering commitee

External review

Layout (Peer-reviewed Journal, Meeting?
Online publication (blog?)?


GITMO BOARD
IBMDR
Barbara Bruno
Sonia Mammoliti
THANKs
AIEOP
AMCLI
AIBT
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SIDEM/SIMTI
ALL TRANSPLANT PROGRAMS
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ADOCES