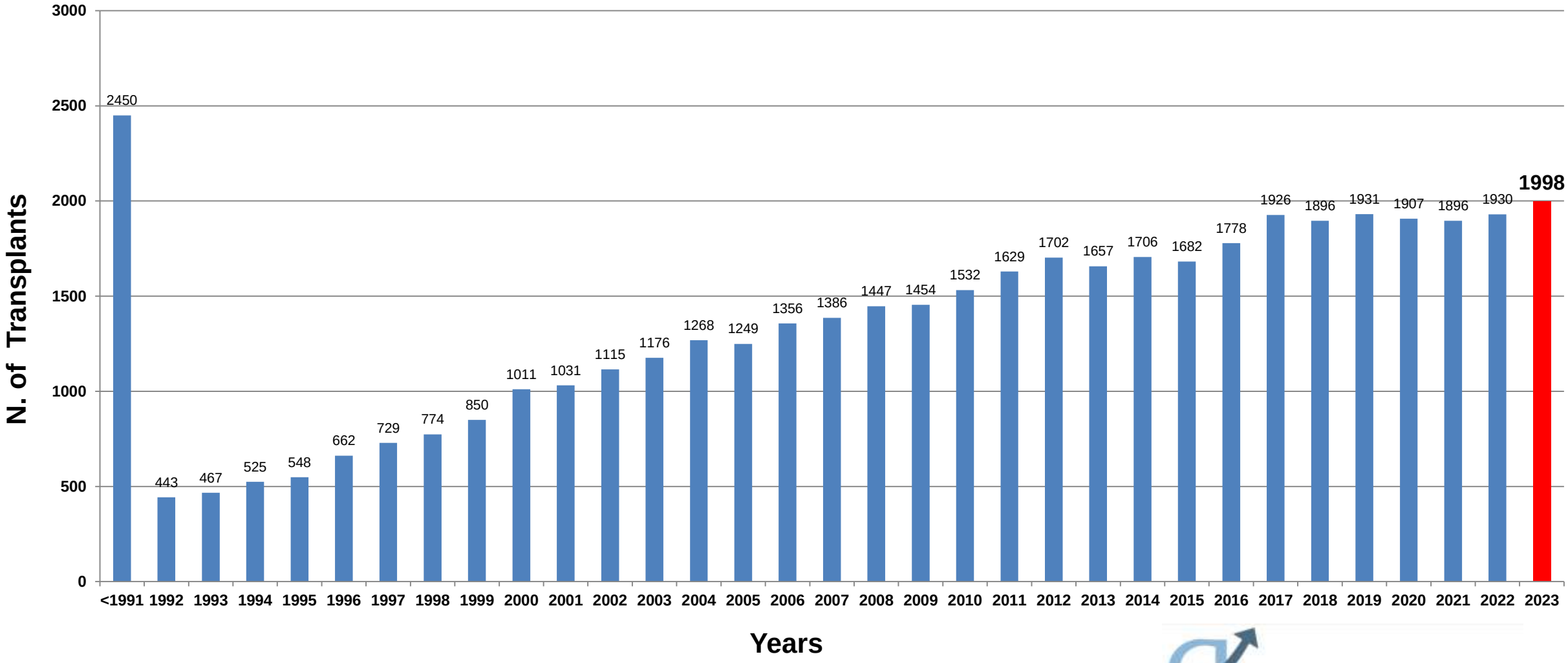
Trapianti e terapie cellulari incluse CAR-T: network GITMO-AIBT ***Massimo Martino***

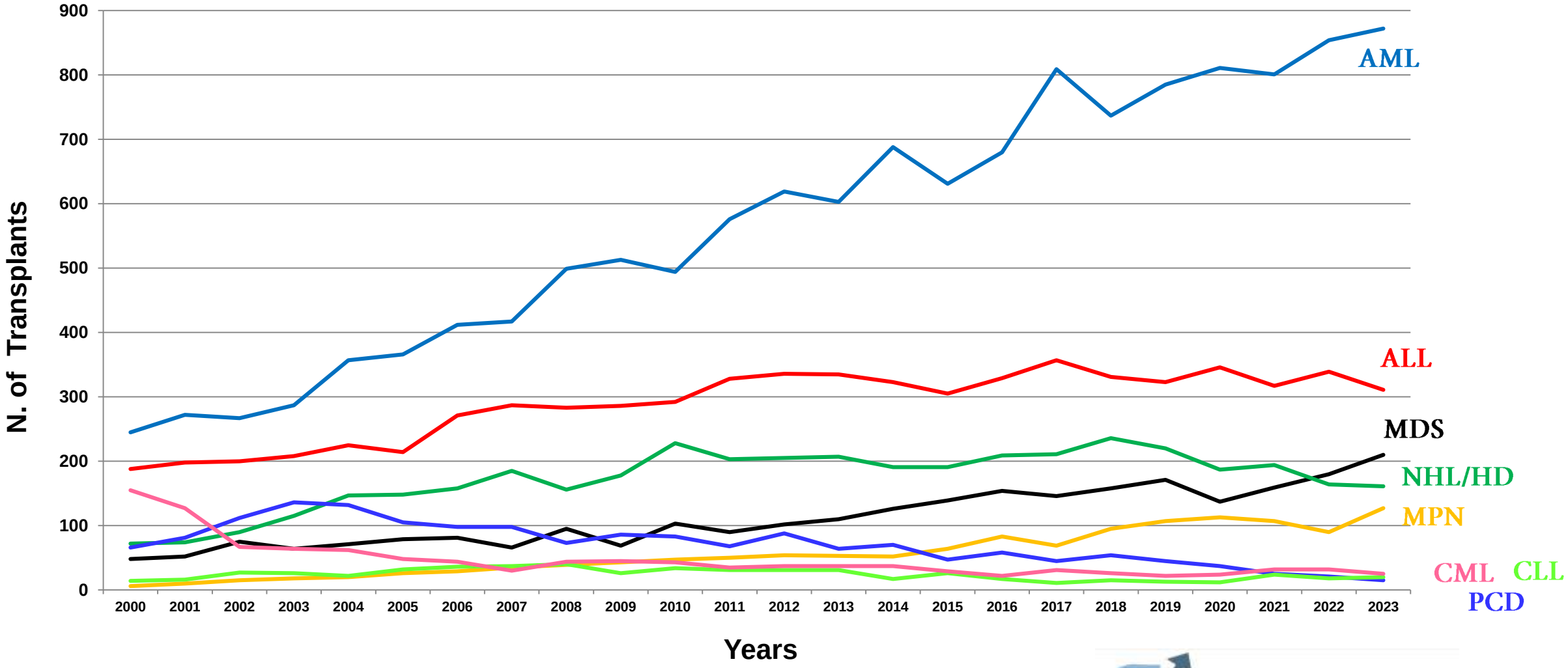
Allogeneic Transplants (n. 45.111)



GITMO

Export date (EBMT Registry) 31/03/2024

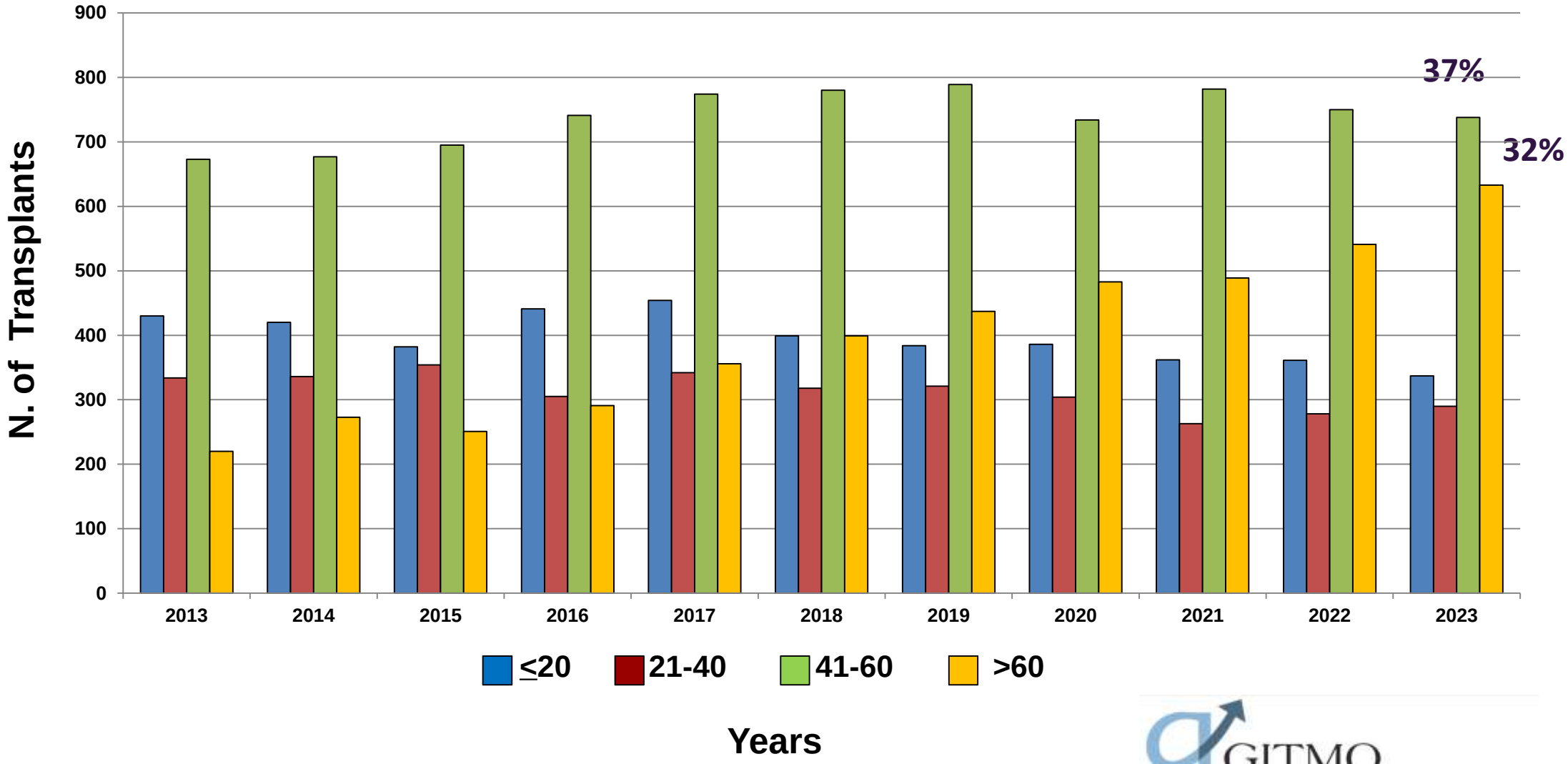
Number of Allogeneic HCTs in Italy by Selected Disease



GITMO

Export date 01/03/2024

2023 - Allogeneic Transplants: Patient age at transplantation



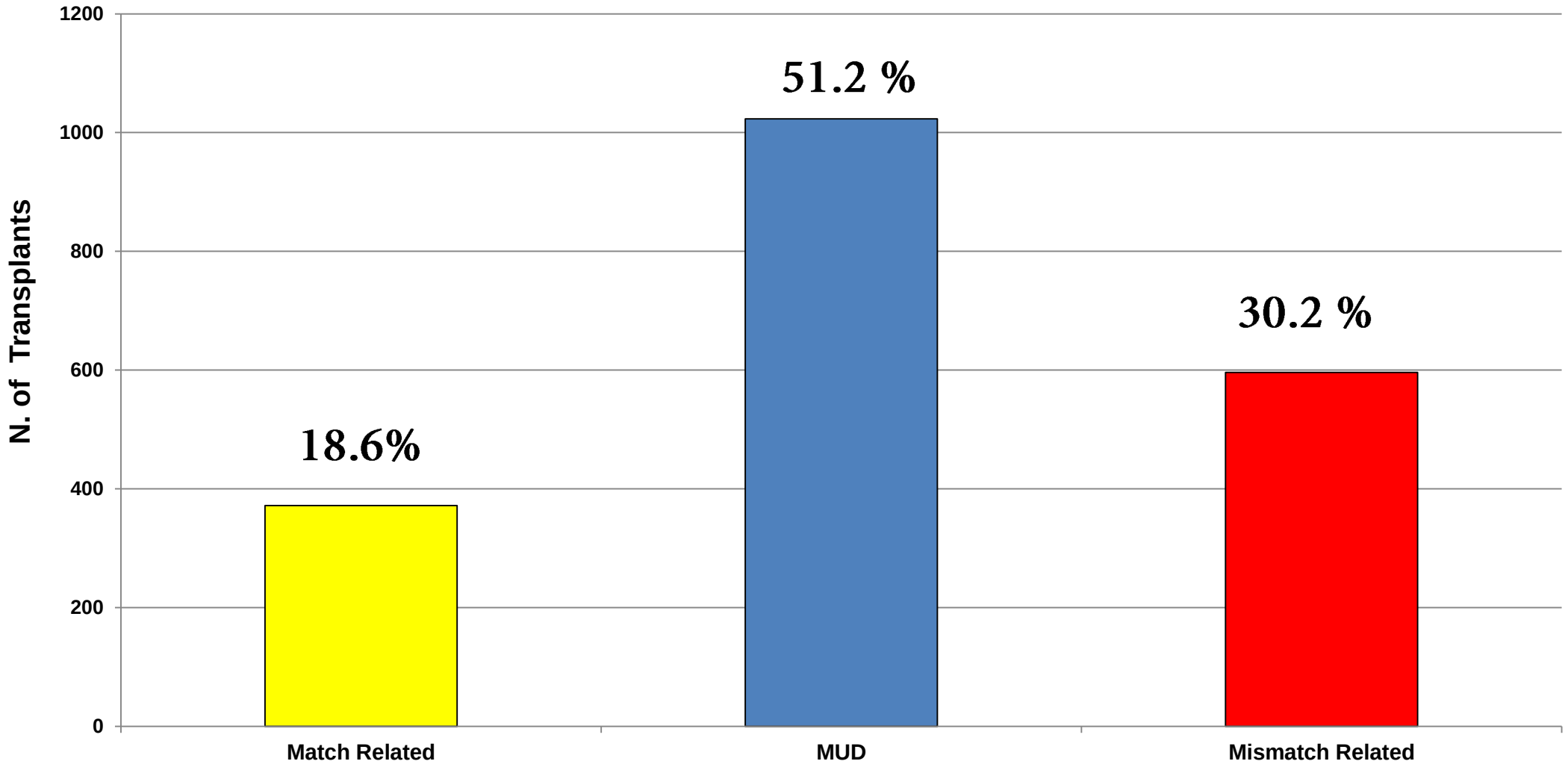
Export date 01/03/2024

Allogeneic Transplants: Number of transplants and patient age

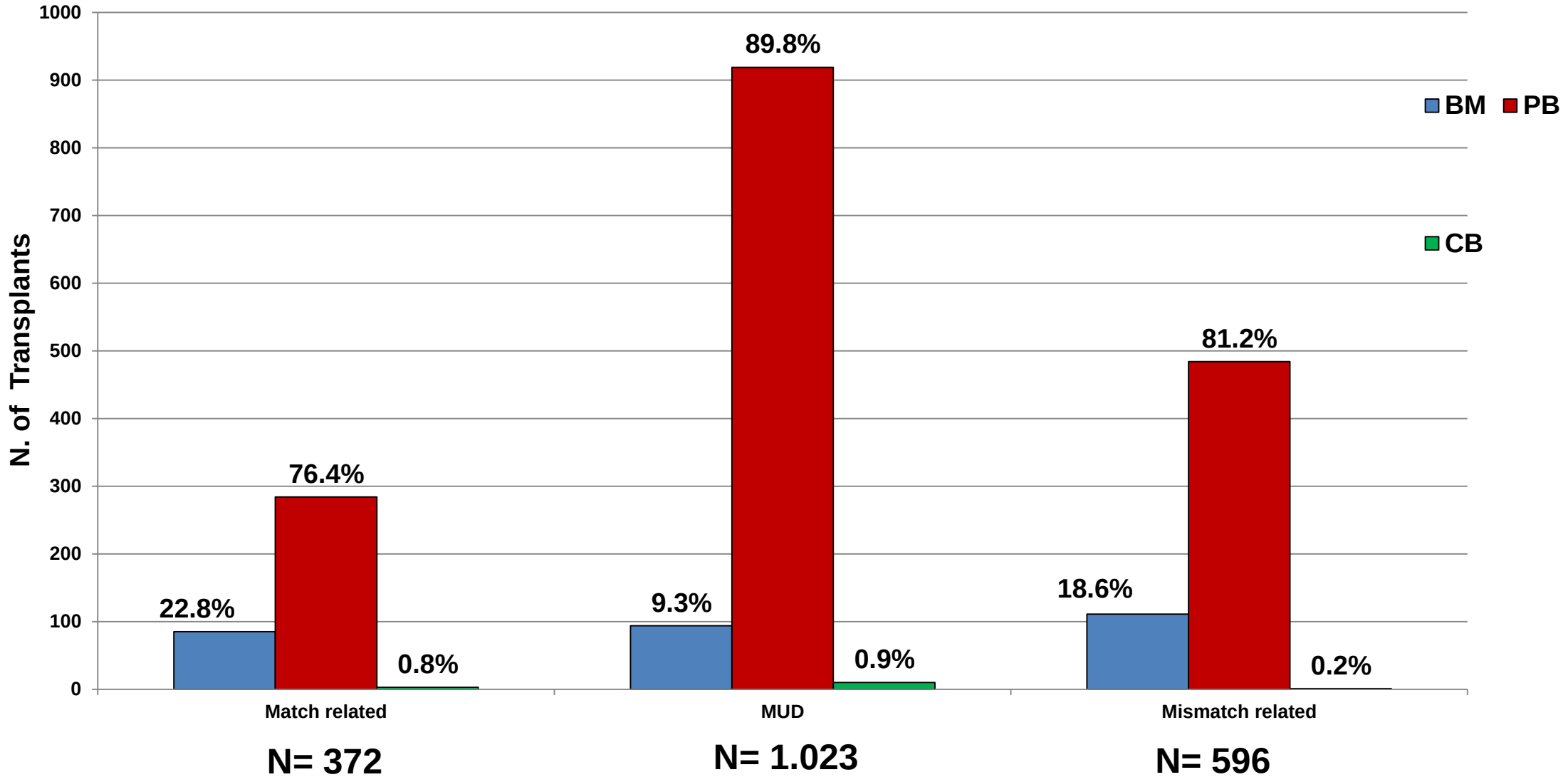
	≤20	21-40	41-60	>60
2013	430	334	673	220
2019	384	321	789	437
2020	386	304	734	483
2021	362	263	782	489
2022	361	278	750	541
2023	337	290	738	633

GITMO

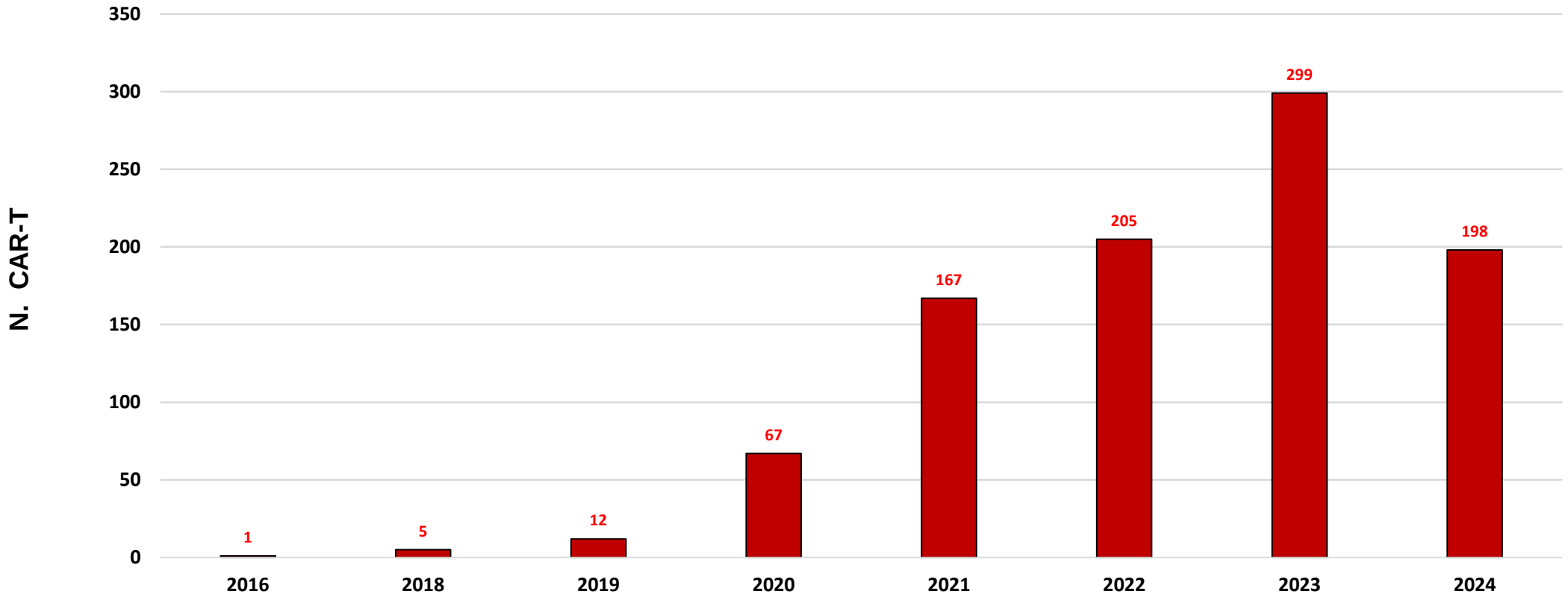
2023 - Allogeneic Transplants (n= 1.998): Donor type



2023 - Allogeneic Transplants: Donor and Source of HSC

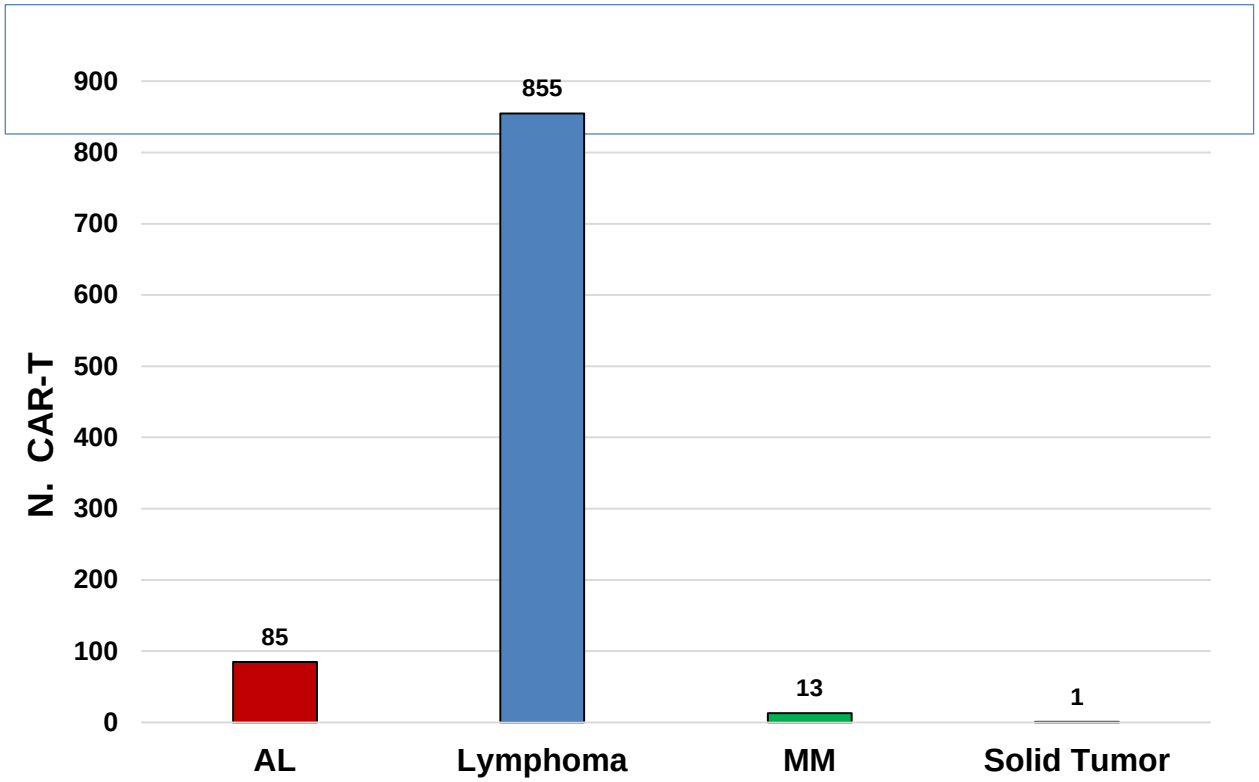


CAR-T procedures by year (n=954)

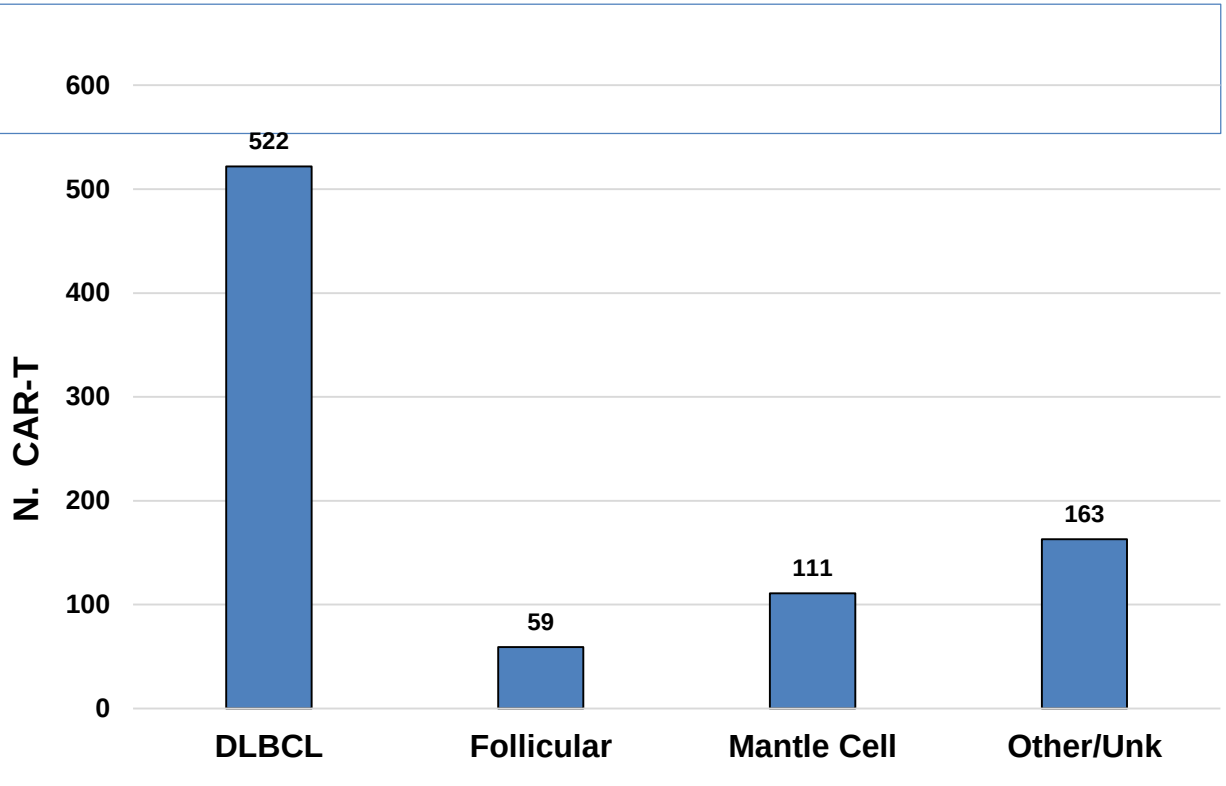


Export date 08/05/2024

CAR-T procedures by disease



Disease

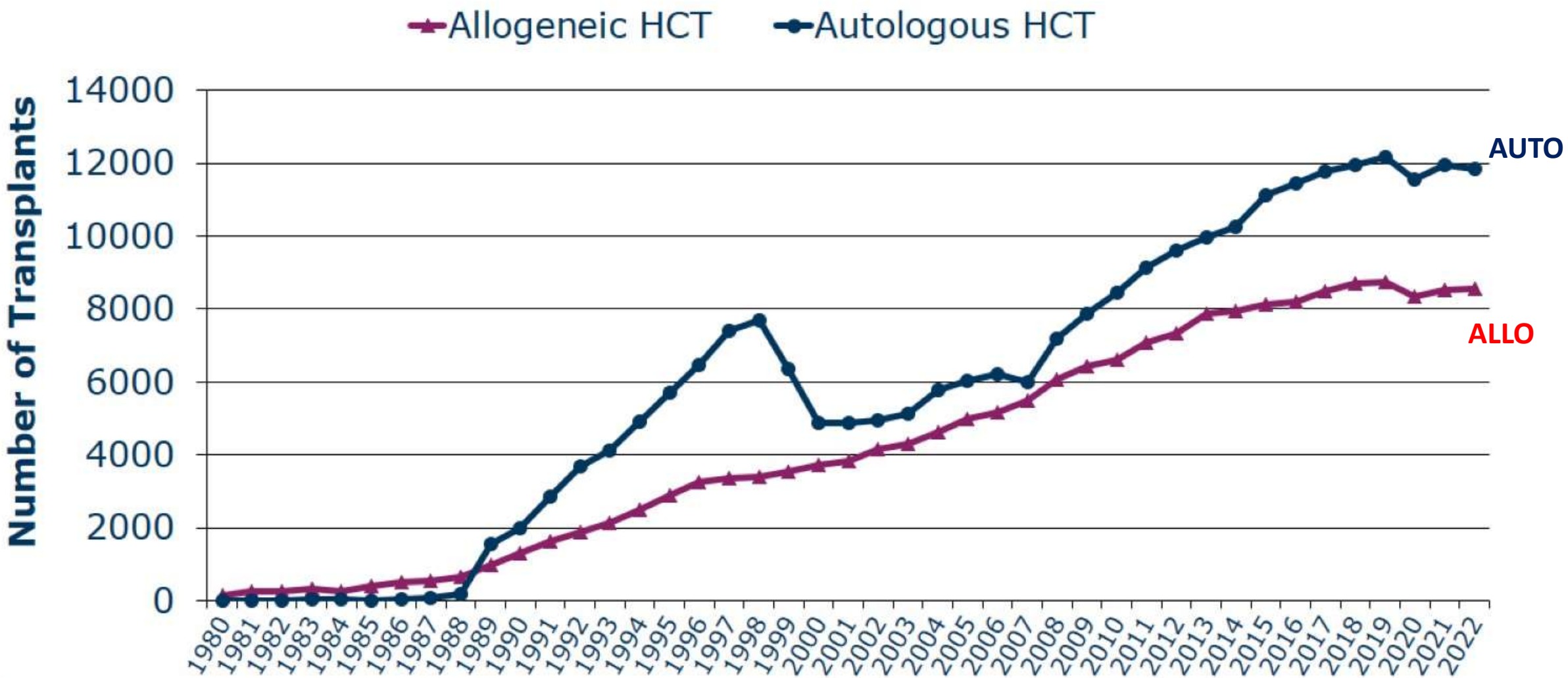


Lymphoma

GITMO

Export date 08/05/2024

Number of 1st HCTs Reported to CIBMTR in the US



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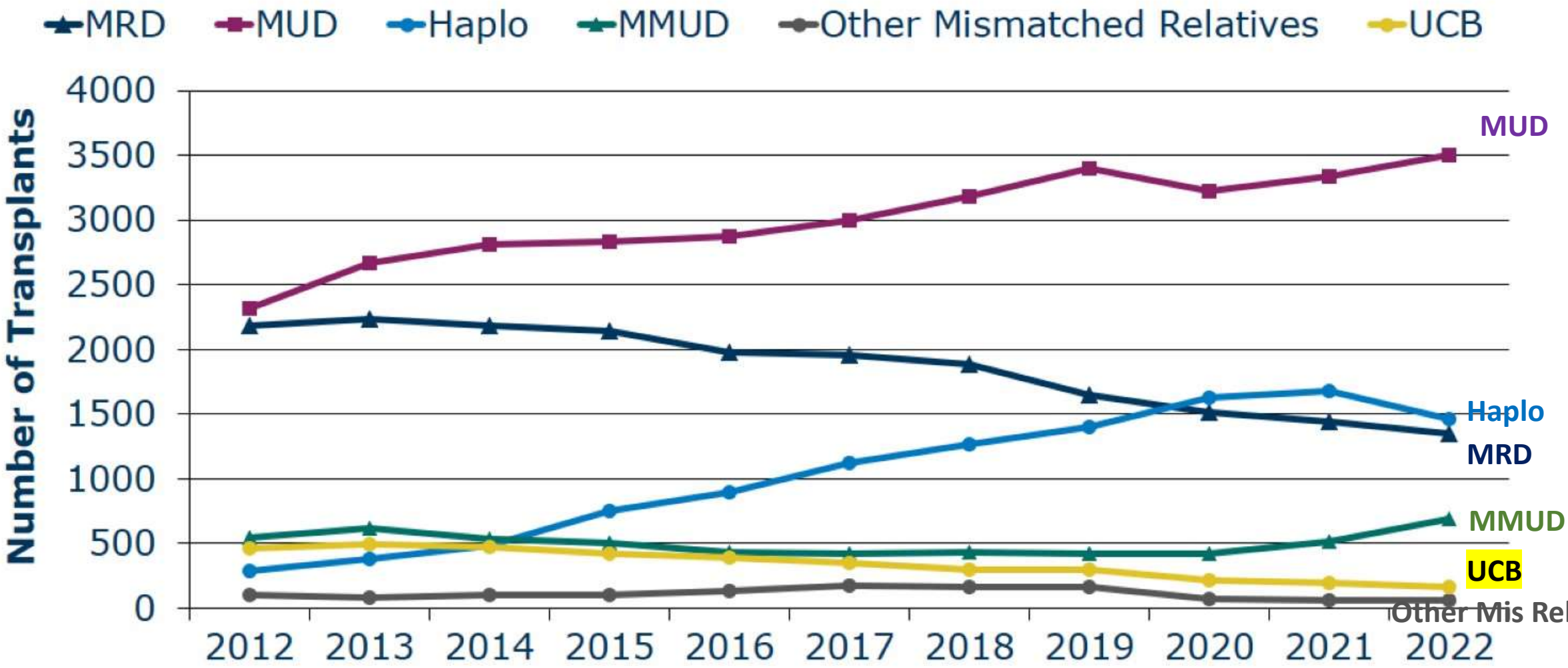
Cusatis R, et al. Transplant Cell Ther. 2024

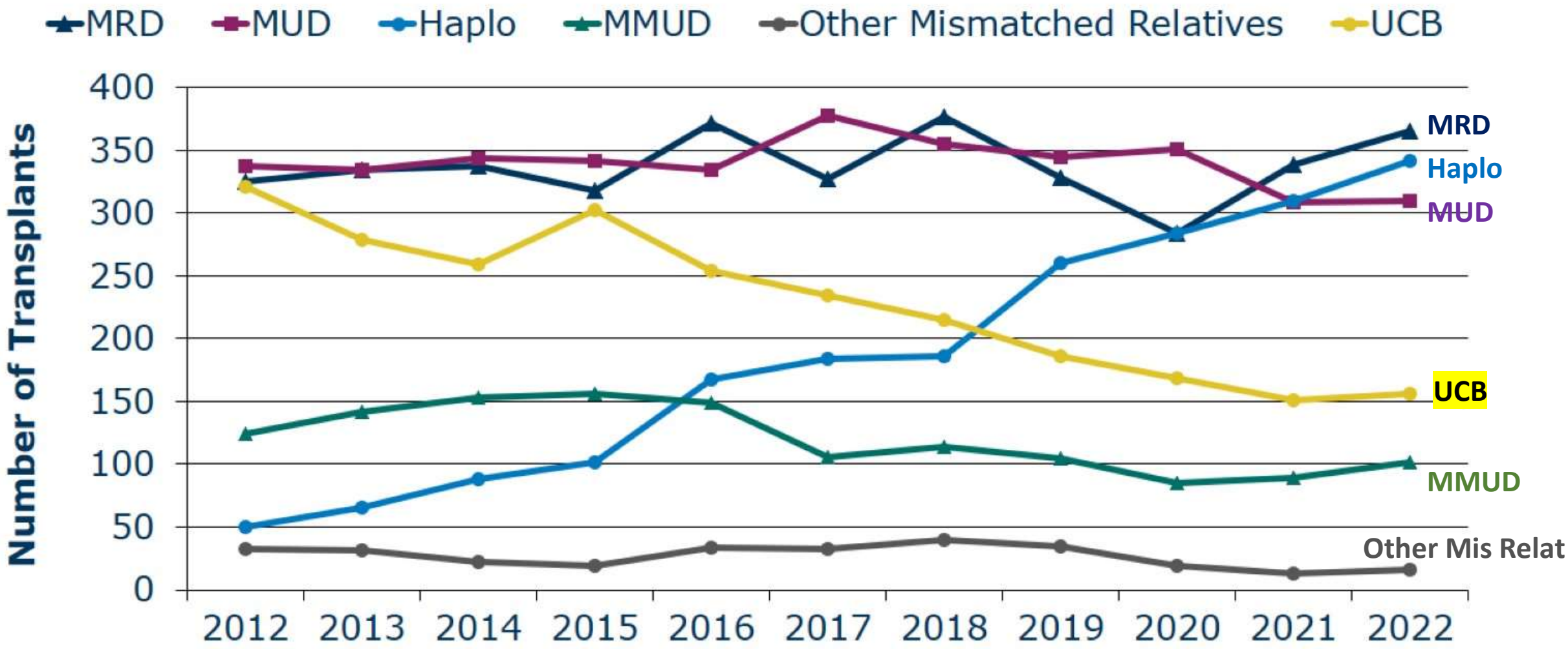
Number of Allogeneic HCTs in the US by Donor Type, Adults



CIBMTR

Abbreviations: MRD, matched related donor; MUD, matched unrelated donor; Haplo, ≥ 2 HLA antigen

Number of Allogeneic HCTs in the US by Donor Type, Pediatrics



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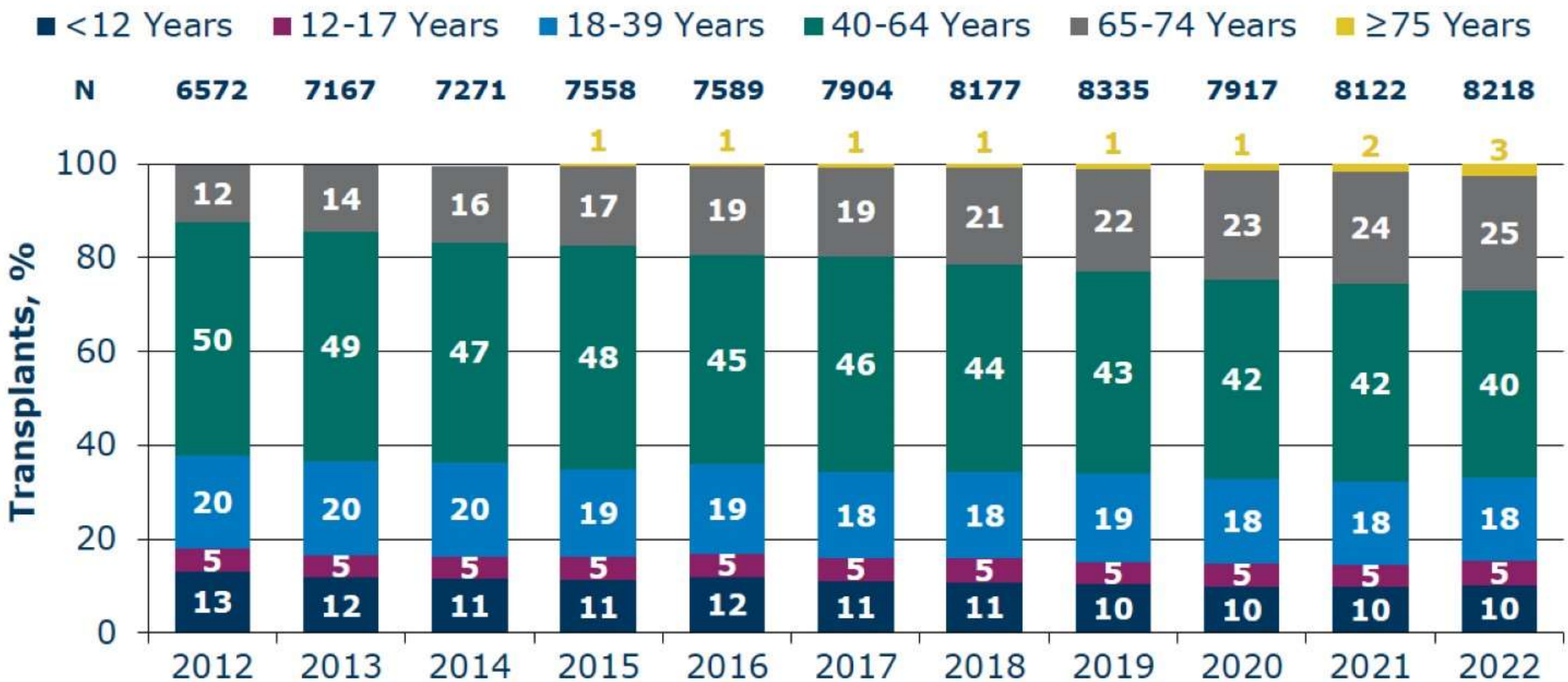
Abbreviations: MRD, matched related donor; MUD, matched unrelated donor; Haplo, ≥ 2 HLA antigen mismatch; MMUD, mismatched unrelated donor ≤ 7/8 HLA allele match; UCB, umbilical cord blood

Recipient Age of Allogeneic HCTs in the US



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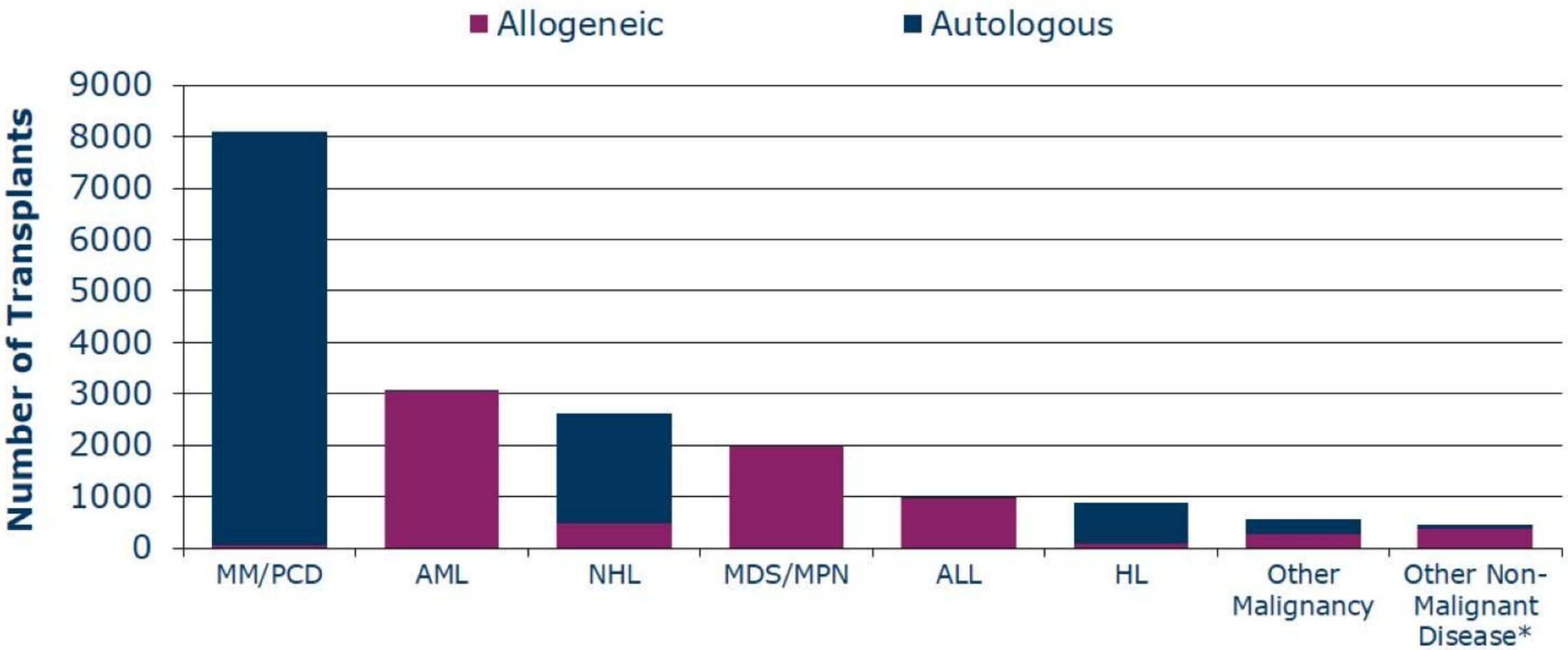
Number of HCTs by Indications in the US, 2022, Adult



*Includes limited gene therapy events

Abbreviations:
ALL, acute lymphoblastic leukemia;
AML, acute myeloid leukemia;
CLL, chronic lymphocytic leukemia;
HL, Hodgkin lymphoma;
MDS, myelodysplastic syndromes;
MM, multiple myeloma;
MPN, myeloproliferative neoplasms;
NHL, non-Hodgkin lymphoma;
PCD, plasma cell disorders.

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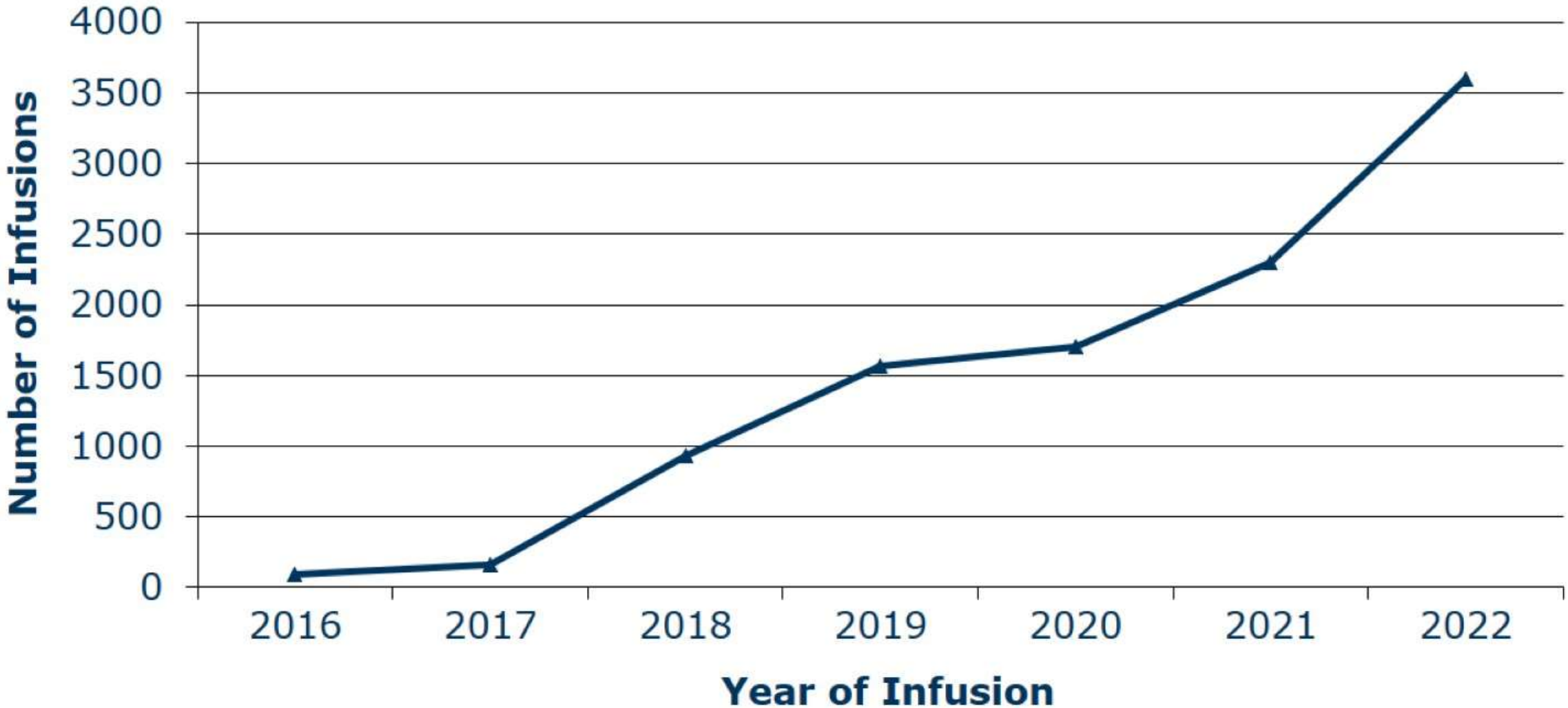
Number of 1st CAR-T Infusions Reported to CIBMTR in the US



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

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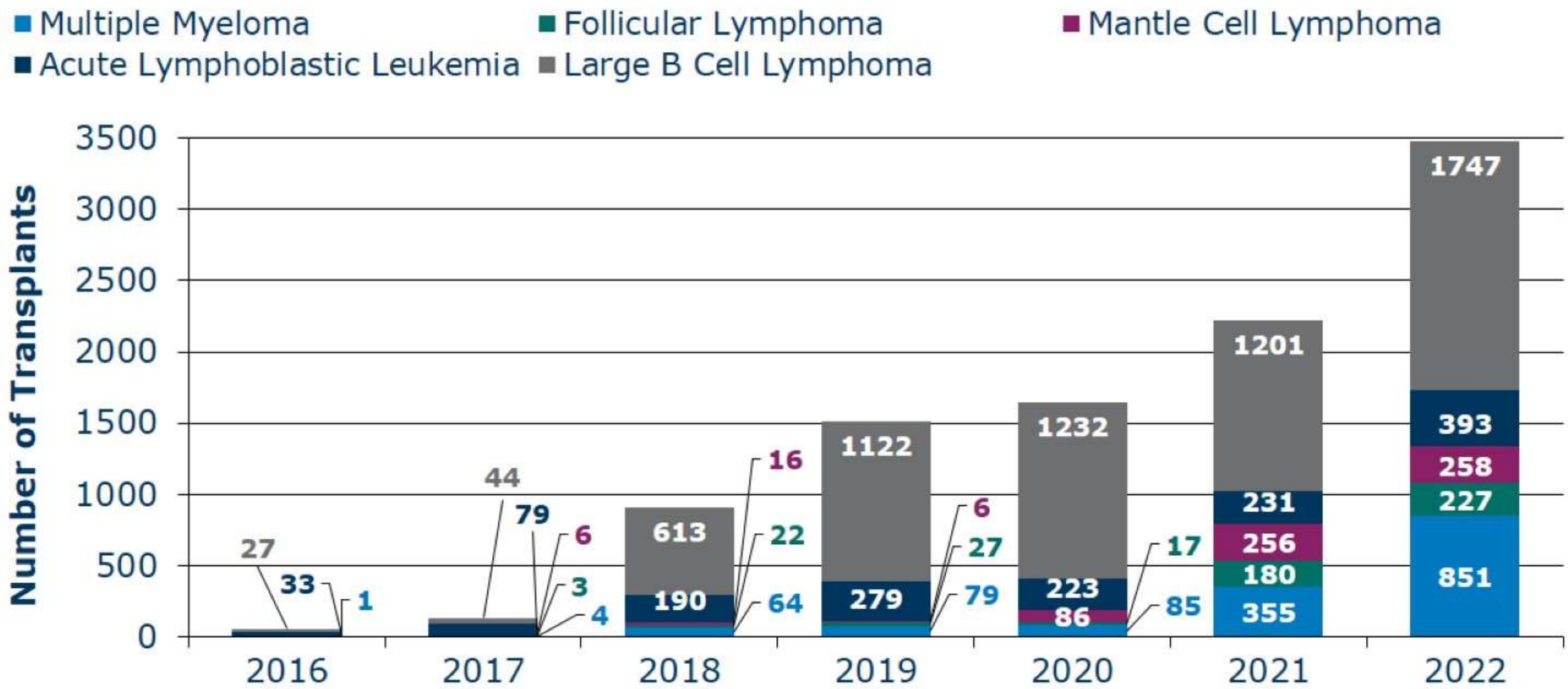
Number of CAR-T Infusions by Indication in the US Annually



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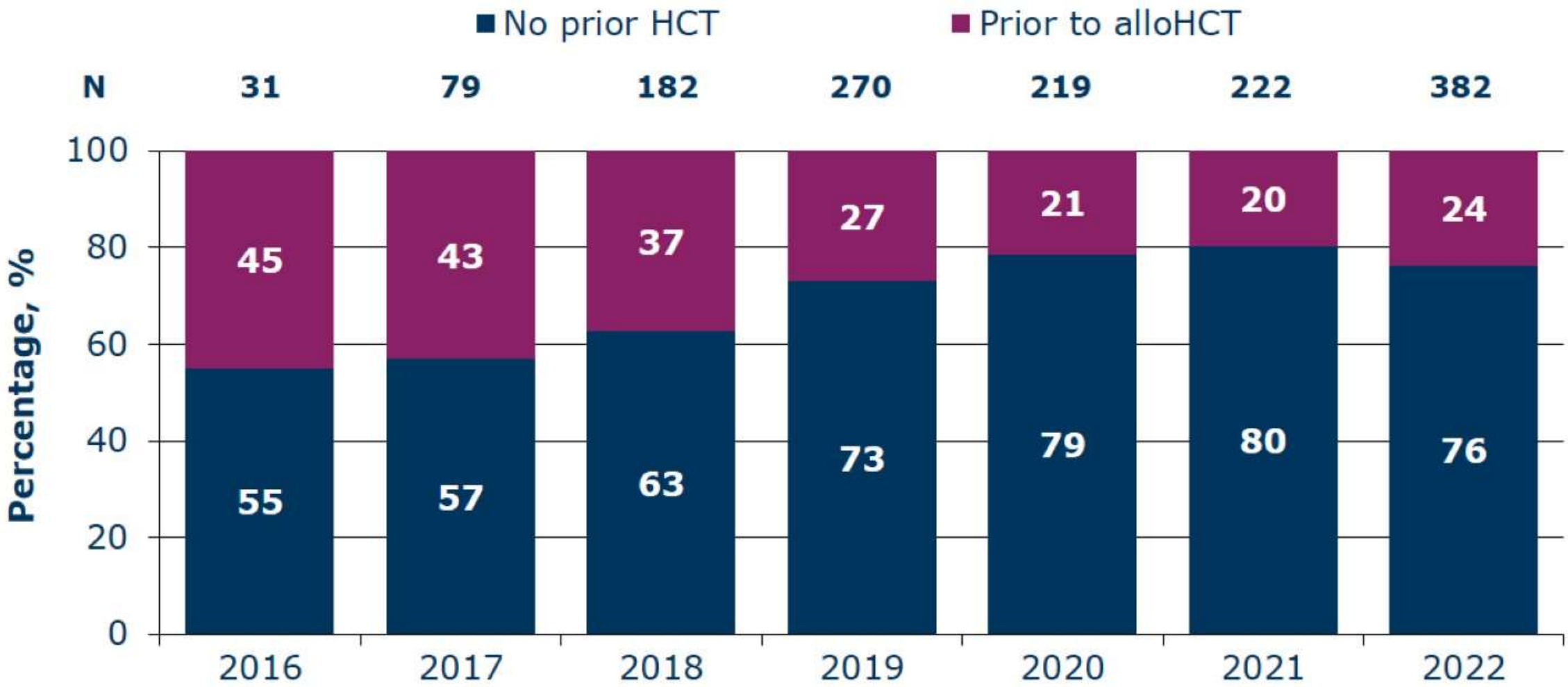
Trends in the use of CAR-T Infusions with Prior Allogeneic HCT for Acute Lymphoblastic Leukemia



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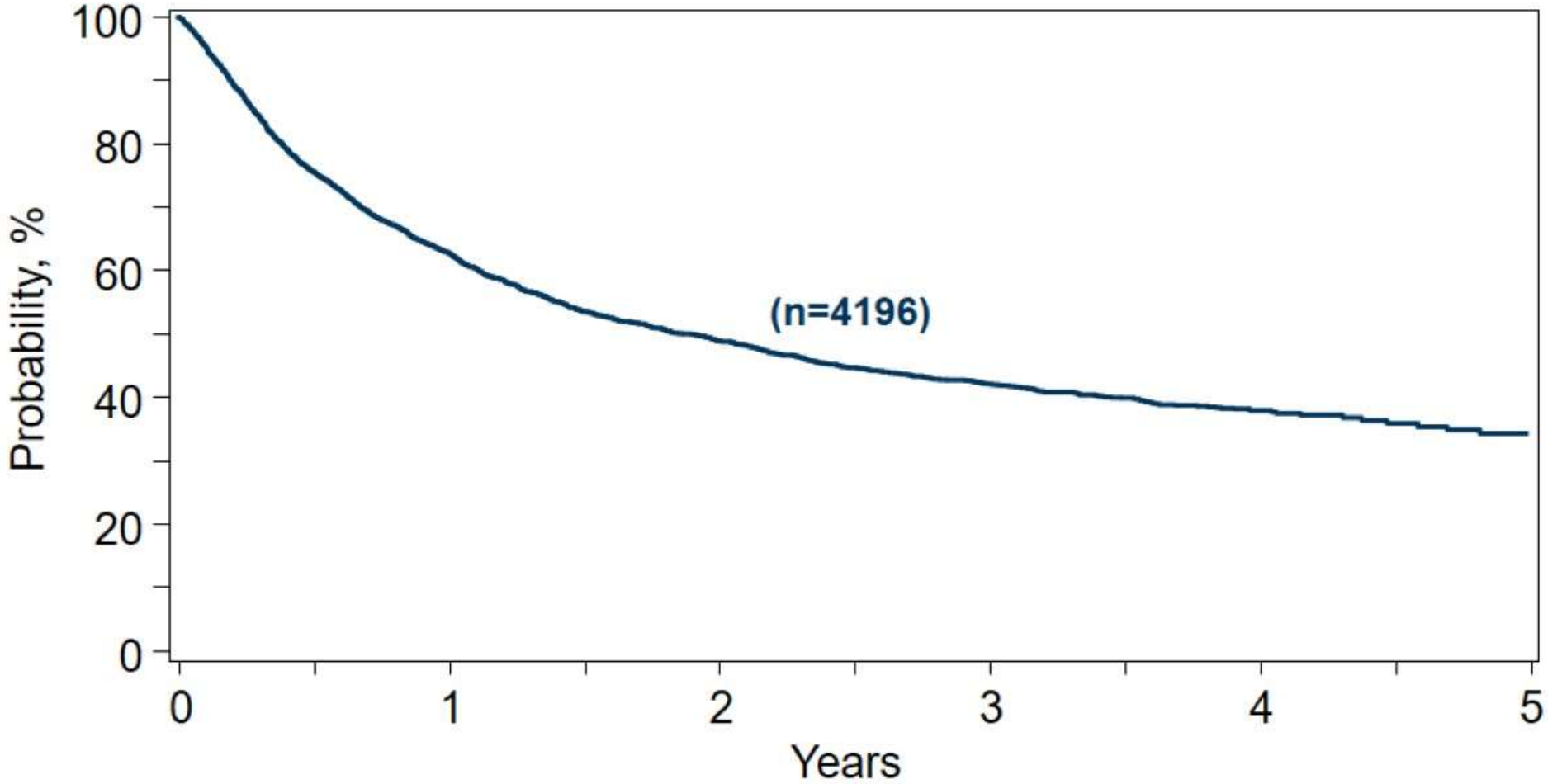
Cusatis R, et al. Transplant Cell Ther. 2024

Survival after First CAR-T Infusion for DLBCL, in the US, 2016-2021



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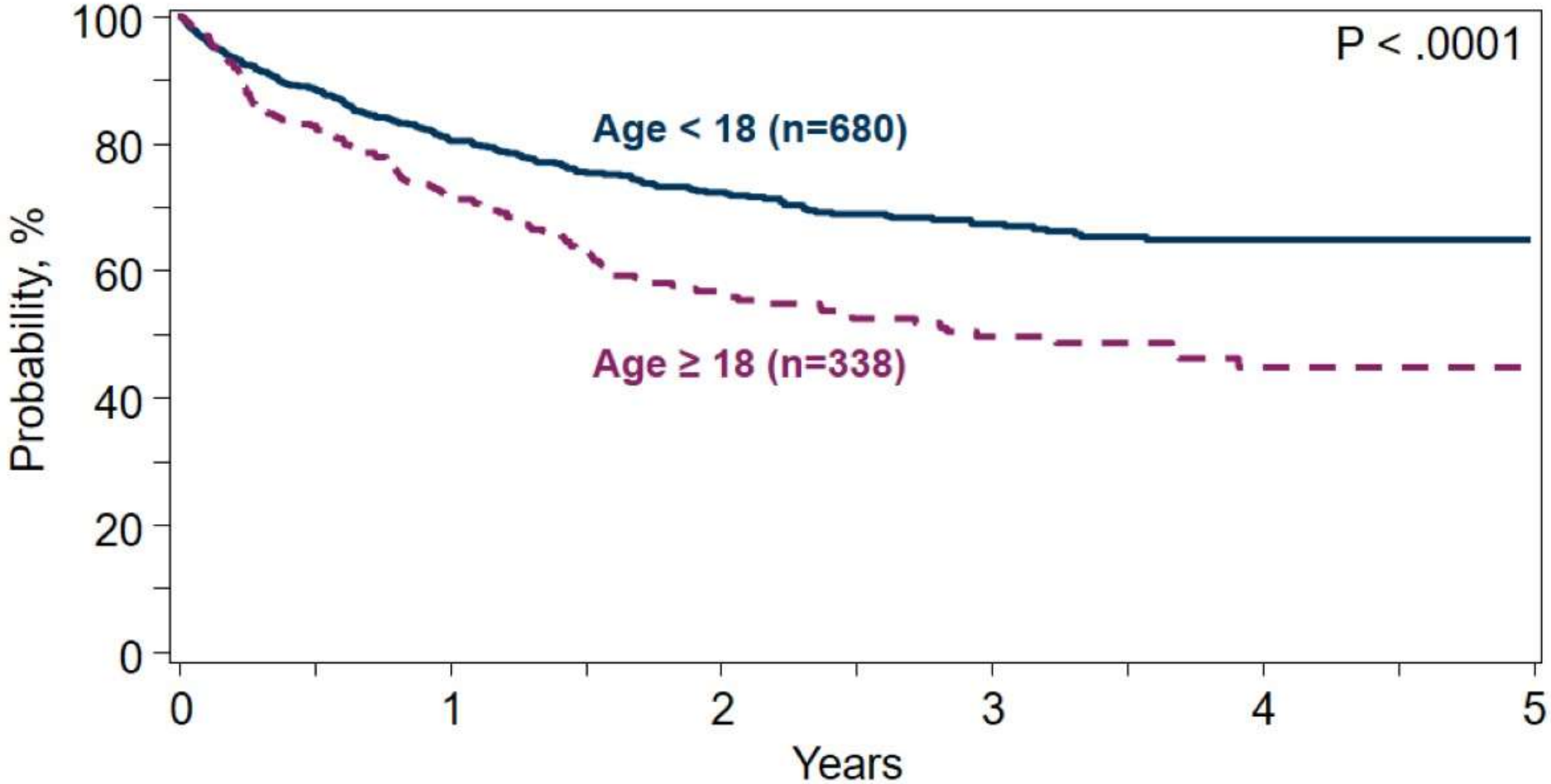
Cusatis R, et al. Transplant Cell Ther. 2024

Survival after First CAR-T Infusion for Acute Lymphoblastic Leukemia, in the US, 2016-2021



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Cusatis R, et al. Transplant Cell Ther. 2024

ARTICLE OPEN

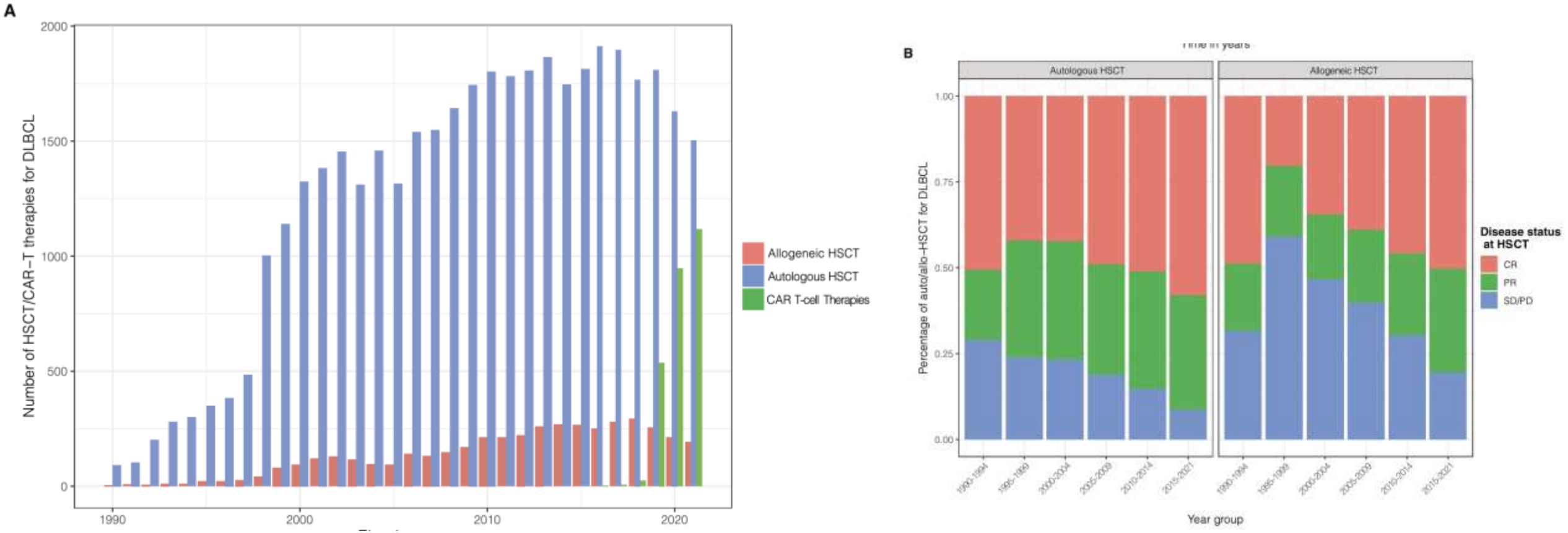
Check for updates

Hematopoietic stem cell transplantation for DLBCL: a report from the European Society for Blood and Marrow Transplantation on more than 40,000 patients over 32 years

Philipp Berning[1], Mathilde Fekom[2], Maud Ngoya[2], Anthony H. Goldstone[3], Peter Dreger[4], Silvia Montoto[5], Hervé Finel[2], Evgenii Shumilov[1], Patrice Chevallier[6], Didier Blaise[7], Tim Strüssmann[8], Ben Carpenter[9], Edouard Forcade[10], Cristina Castilla-Llorente[11], Marek Trneny[12], Hervé Ghesquieres[13], Saveria Capria[14], Catherine Thieblemont[15], Igor Wolfgang Blau[16], Ellen Meijer[17], Annoek E. C. Broers[18], Anne Huynh[19], Denis Caillot[20], Wolf Rösler[21], Stephanie Nguyen Quoc[22], Jörg Bittenbring[23], Arnon Nagler[24], Jacques-Emmanuel Galimard[2], Bertram Glass[25], Anna Sureda[26,27] and Norbert Schmitz[1,27]✉

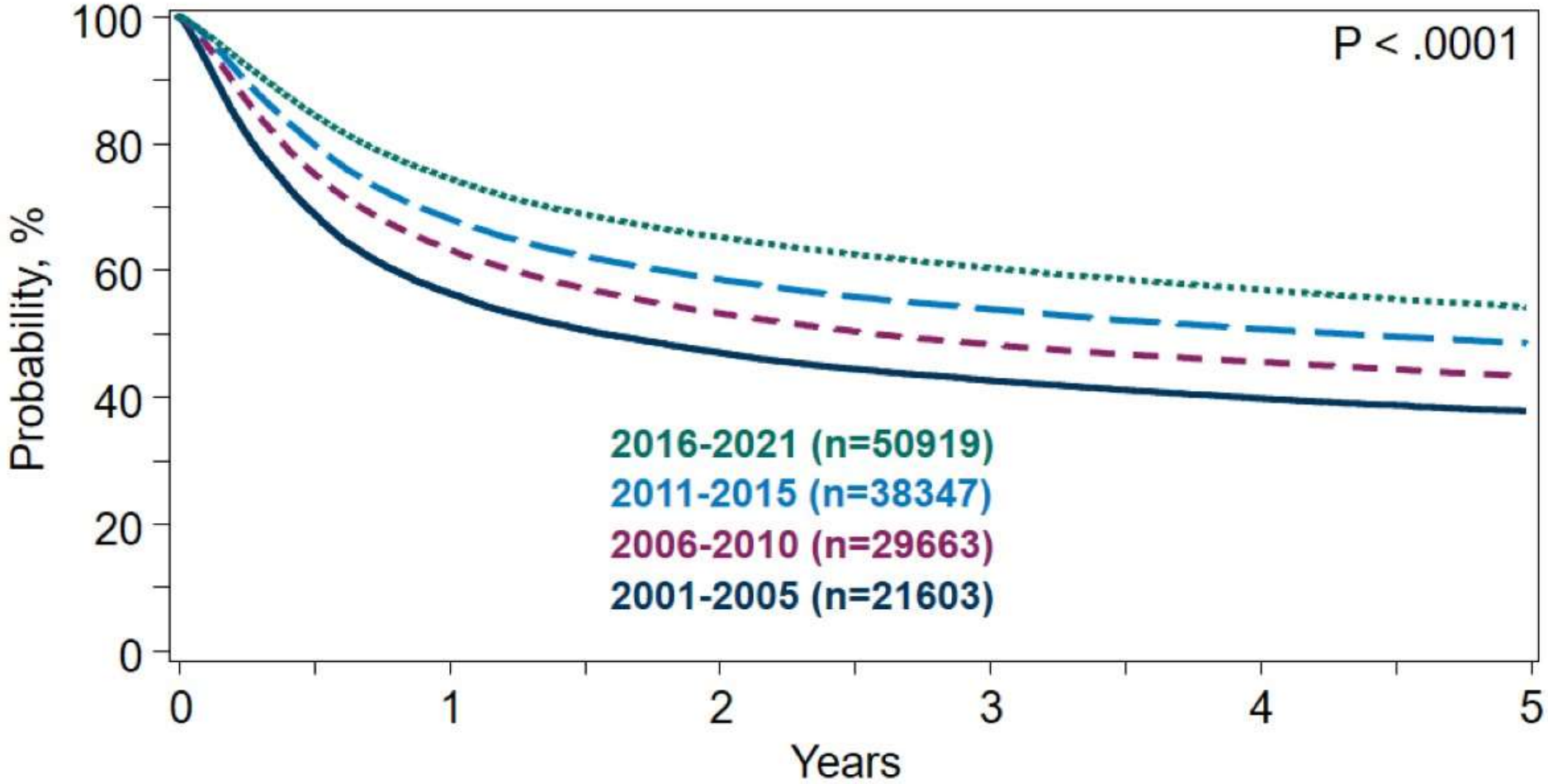
Berning, P., Fekom, M., Ngoya, M. *et al.* Hematopoietic stem cell transplantation for DLBCL: a report from the European Society for Blood and Marrow Transplantation on more than 40,000 patients over 32 years. *Blood Cancer J.* **14**, 106 (2024).

Trends for hematopoietic stem cell transplantation and CAR T-cell infusions for DLBCL over time



Berning, P., Fekom, M., Ngoya, M. *et al.* Hematopoietic stem cell transplantation for DLBCL: a report from the European Society for Blood and Marrow Transplantation on more than 40,000 patients over 32 years. *Blood Cancer J.* **14**, 106 (2024).

Trends in Survival after Allogeneic HCTs, in the US, 2001-2021



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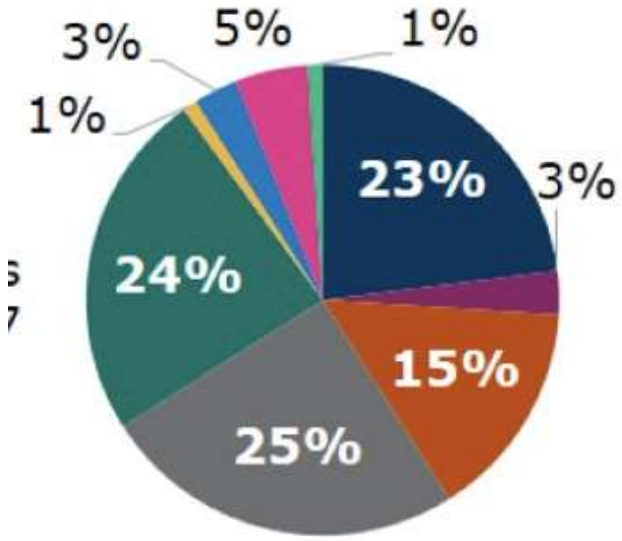
Cusatis R, et al. Transplant Cell Ther. 2024

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

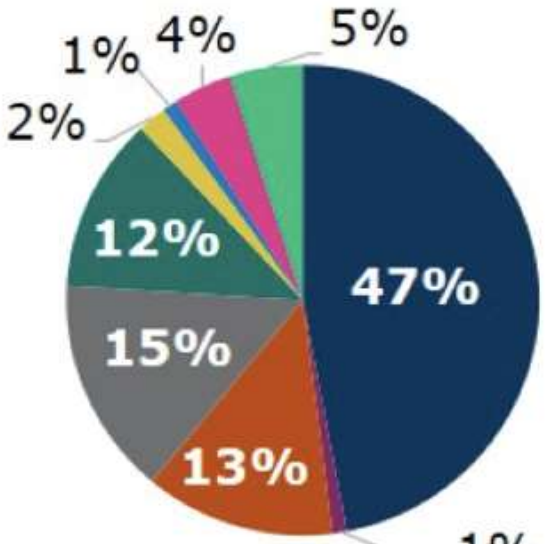
Died within 100 days post-transplant



n=7133

9.4 %

Died at or beyond 100 days post-transplant*



n=27505

36.4 %

- Primary disease
- Organ failure
- Hemorrhage
- Graft rejection
- GVHD
- Infection
- Malignancy subsequent to HCT
- Other
- Not reported

*Data reflects 10-year mortality.

Age ≥18 years
Total transplants = 75507

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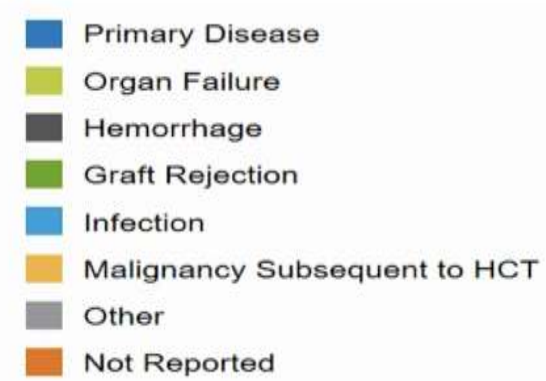
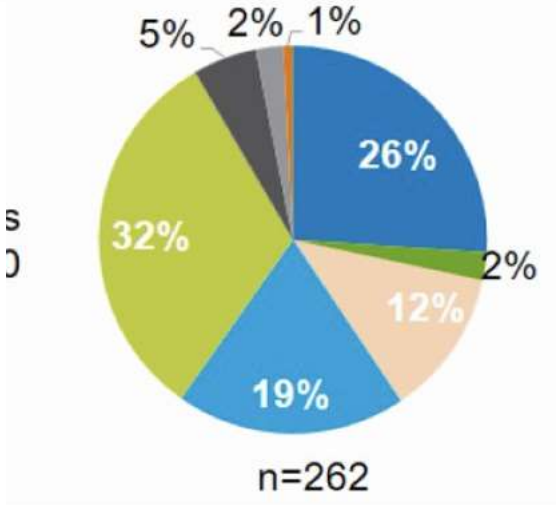
Causes of Death within 100 days post-transplantiation the U.S. -2018-2020



Matched Related Donor

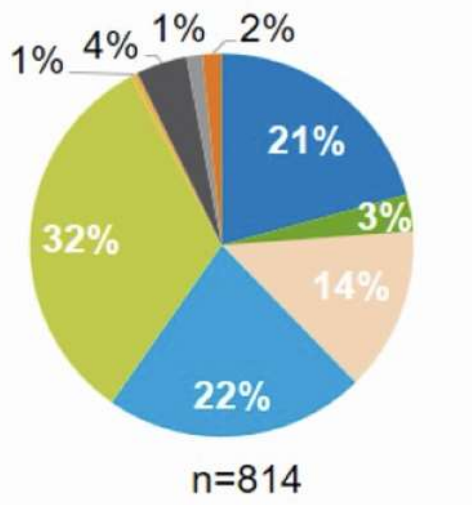


n=262

TRM= 5.3%

Age ≥18 years
Total transplants = 4930

Matched Unrelated Donor

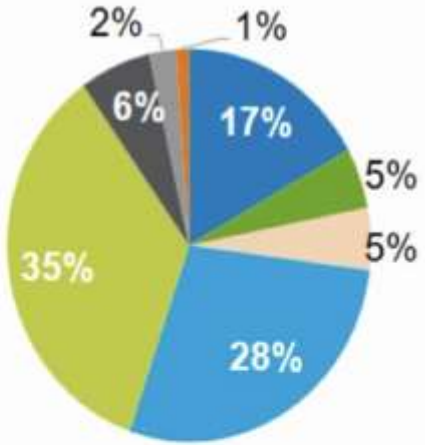


n=814

TRM= 8.3%

Age ≥18 years
Total transplants = 9776

Haplo Donor

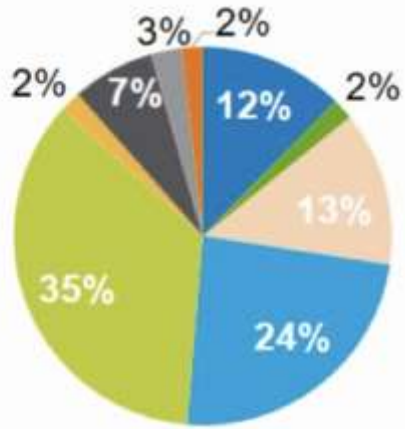


n=426

TRM 9,8 %

Age ≥18 years
Total transplants = 4336

Mismatched Unrelated Donor

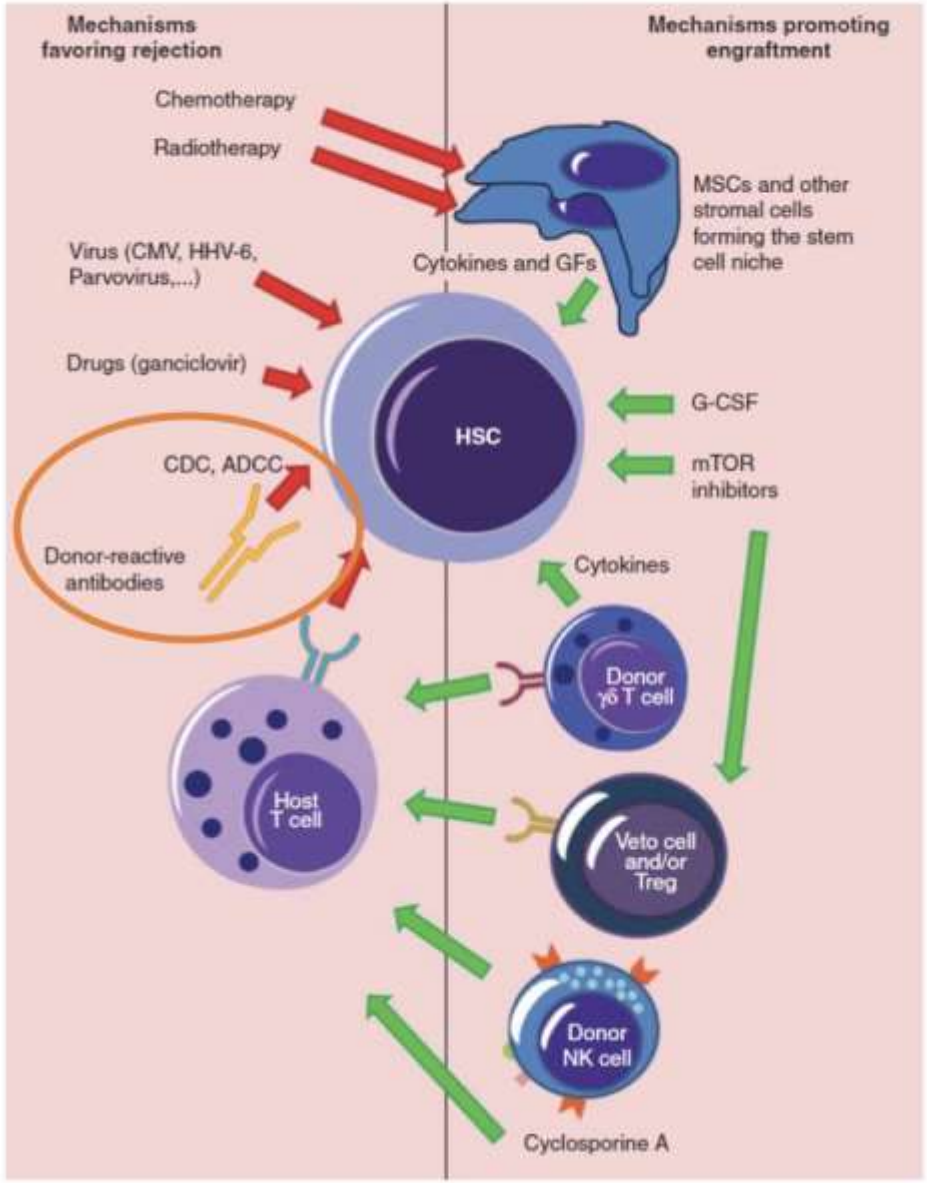


n=113

TRM= 14.1%

Age ≥18 years
Total transplants = 1281

Graft failure



RISK FACTORS

- HLA mismatches
- Nonmalignant disease (↑↑ SAA, Haemoglobinopathies)
- Advanced disease
- Graft source (UCB)
- Conditioning (NMA/RIC)
- T-cell depletion
- Anti-HLA antibodies
- Extensive marrow fibrosis extensive prior treatment
- Donor age
- ABO mismatch
- Splenomegaly
- Cell dose
- Viral infections
- GVHD
- Drug toxicity
- Iron overload
- Transfusion history

F. Locatelli et al, Expert Opin Pharmacother. 2014
D. Valcárcel and A. Sureda, EBMT Handbook 2019

Donor Specific Antibodies (DSA)

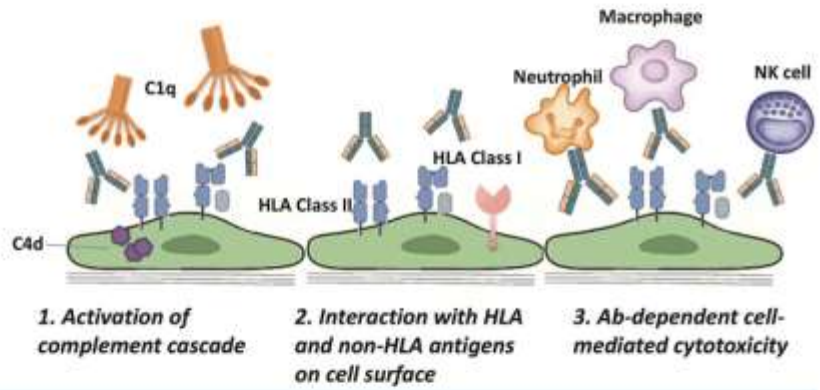
Preformed antibodies in the recipient directed against the candidate donor's class I and/or class II HLA antigens

Formation of antibodies to allogeneic HLA antigens after exposure to foreign cells or tissue through:

- *Pregnancy*
  - -Result of sensitization during pregnancies by offspring's HLA antigens
  - -Risk with a higher number of pregnancies (reported incidence up to 50% in the female recipient with a history of multiple pregnancies)[1]
- *Blood product transfusion*[2]
- *Previous transplantation*[3]

Rate of HLA sensitization in HSCT candidates: 20% to 40%[3-7]

Rate of DSA to at least one potential donor: 1.4% to 24%[3-7]



Hematopoietic Stem Cell Transplantation (Graft Failure, Poor Graft Function, Delayed Engraftment)

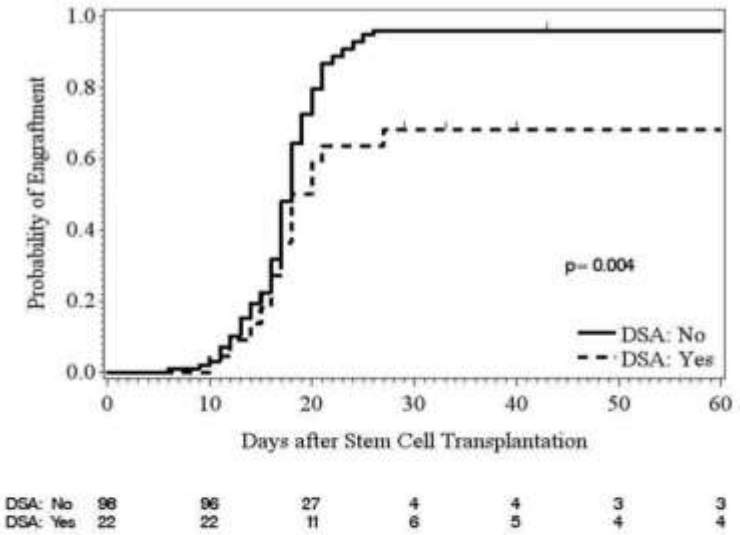
Tranfusion medicine (Tranfusion refractoriness, TRALI)

Solid Organ Transplantation (Hyperacute, acute, chronic rejection)

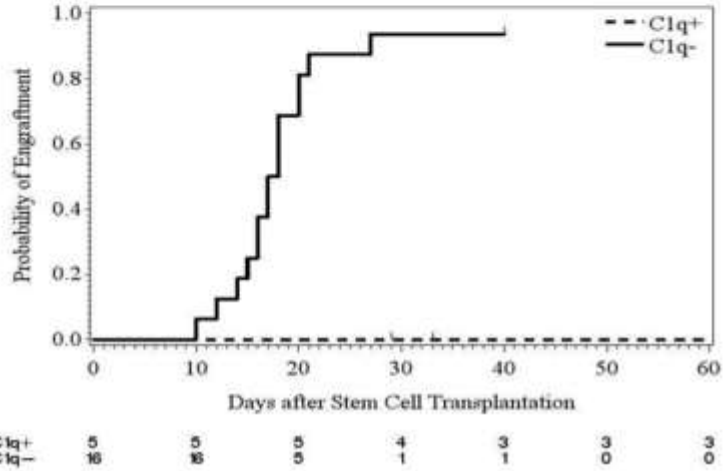
[1] L. Morin-Papunen L et al, Med Biol 1984. [2] M.D. Seftel et al, Blood 2004. [3] S. Yoshihara et al, Bone Marrow Transplant 2012. [4] Y.-J. Chang, et al, J. Hematol. Oncol 2015. [5] S. Spellman et al. Blood 2010. [6] H. Yamamoto et al, Biol. Blood Marrow Transplant 2014. [7] D.E. Gladstone et al, Biol. Blood Marrow Transplant 2013.

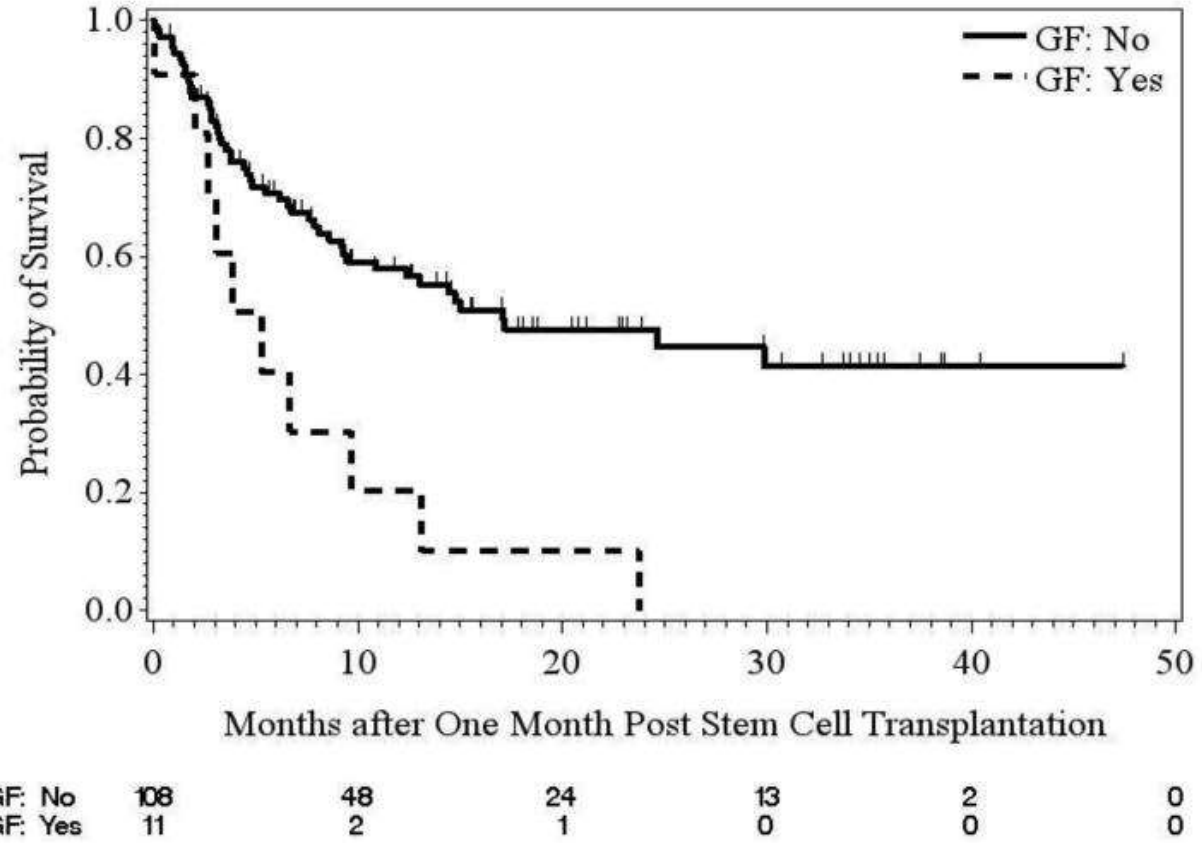
DSA are associated with a higher incidence of GF and poor survival

A.



B.





S.O. Ciurea et al, BBMT 2015

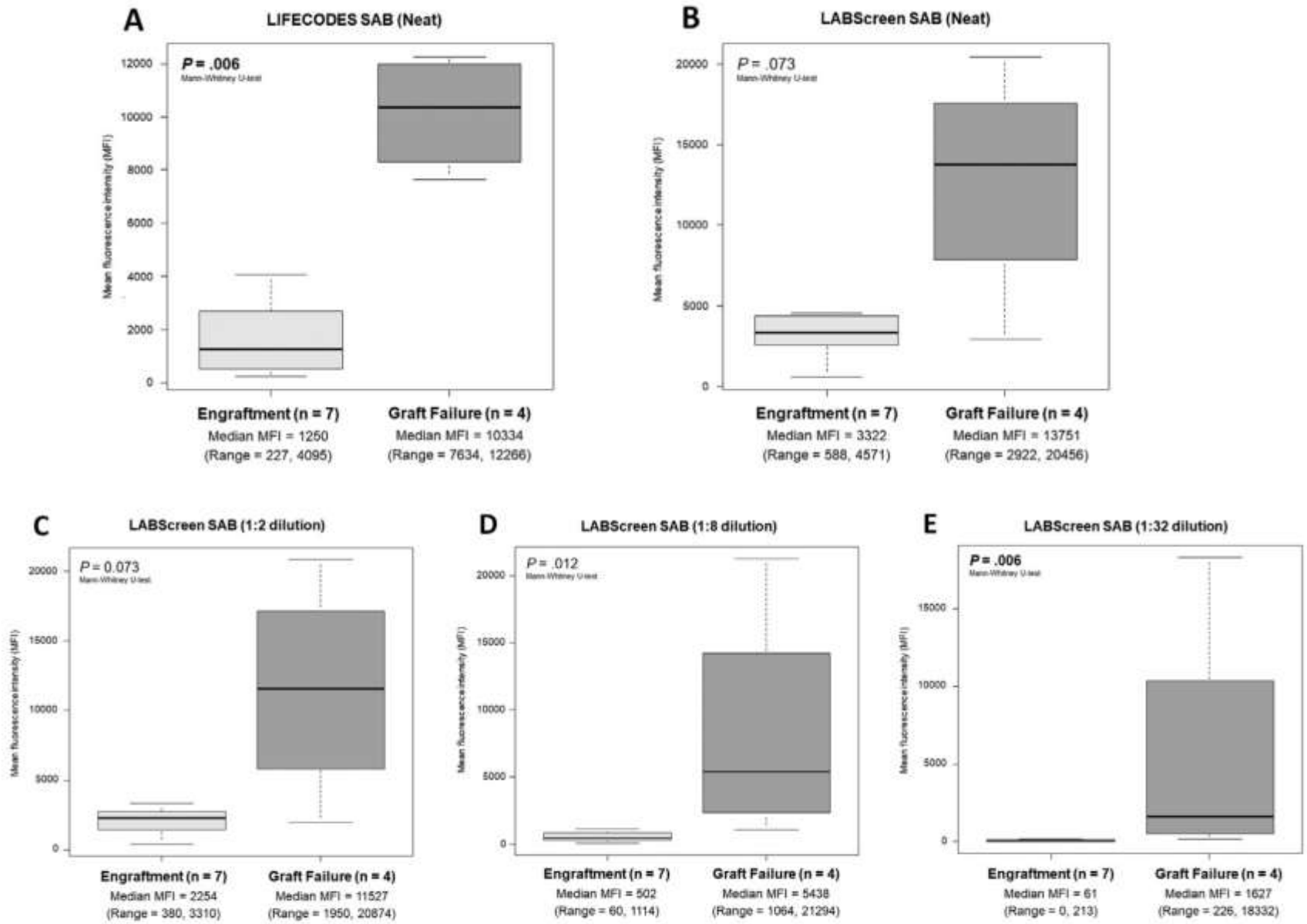
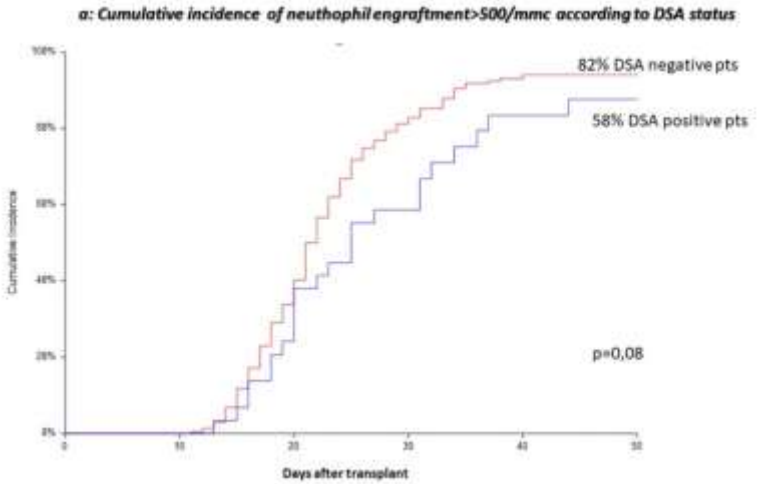


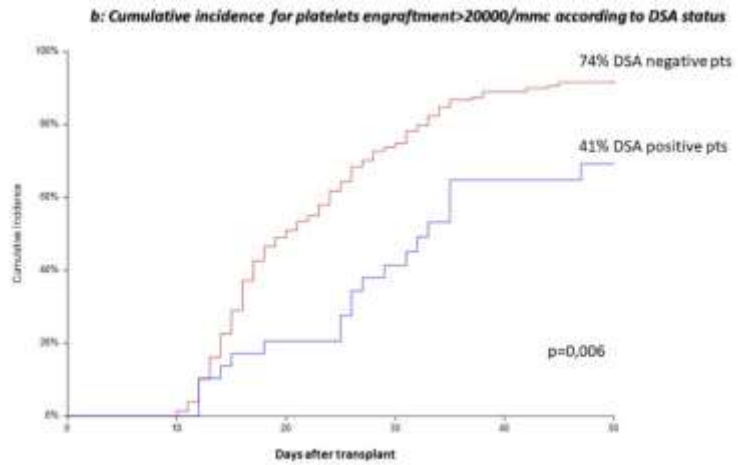
Figure 2. Median MFI values in DSA-positive patients with and without GF: LIFECODES SAB with neat serum (A), LABScreen SAB with neat serum (B), 1:2 dilution (C), 1:8 dilution (D), and 1:32 dilution (E).

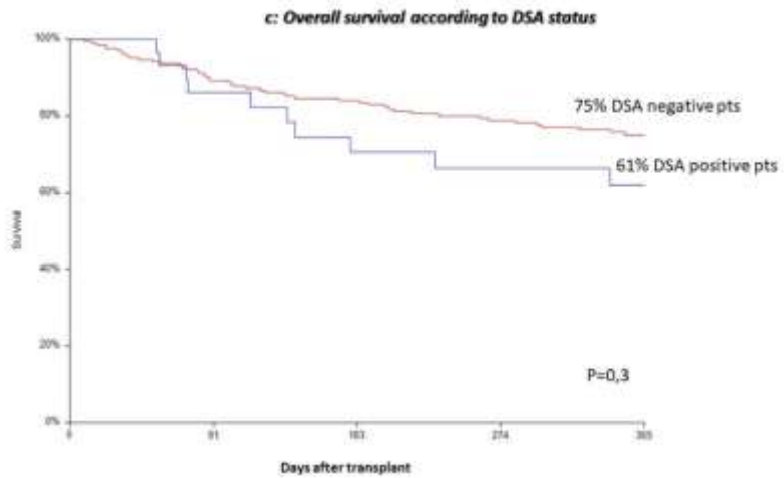
TABLE 1 Patients' characteristics.

Patients (n)	**236**
Median age (range)	56 years (range 19–74 years)
Gender	M/F = 139/97
Diagnosis – Acute leukemia/MDS – Lymphoproliferative disease – Chronic myeloproliferative disease – Aplasia	 – 148 (63%) – 24 (10%) – 52 (22%) – 12 (5%)
Disease status before HCT – Complete remission – Stable disease – Progressive disease – HCST frontline	 – 114 (48%) – 97 (41%) – 23 (10%) – 4 (1%)
Conditioning regimen – Myeloablative – Reduced intensity – CTX	 – 153 (64%) – 83 (35%) – 1 (4%)
Donor – MUD 7/8 – MUD 8/8 – SIB – HAPLO – CB	 – 41 (17%) – 86 (36%) – 38 (16%) – 68 (30%) – 3 (1%)
GvHD prophylaxis – CSA, CTX, MMF – CSA, CTX, MTX, ATG	 – 232 (98%) – 4 (2%)
CD34+ cell median (range)	5.9×10^6/kg (1.6–15)
Acute GvHD grade >/=2	57 (24%)
Chronic GvHD grade >/=2	23 (10%)
Presence of anti HLA antibodies	29 (12%)

CTX, cyclophosphamide; CSA, cyclosporine; MMF, mycophenolic acid; MTX, methotrexate; ATG, anti-thymocyte globulin.







Sica S, et al. Front Oncol. 2024

> Curr Res Transl Med. 2024 Sep;72(3):103464. doi: 10.1016/j.retram.2024.103464.
Epub 2024 Aug 17.

Impaired survival of patients with non donor-specific anti-HLA antibodies before HLA-mismatched allogeneic stem cell transplantation

Antonio Milano [1], Giuliana Lando [1], Giulia Di Maggio [1], Giorgia Cornacchini [1], Giovanni Grillo [2], Roberto Cairoli [2], Silvano Rossini [1], Roberto Crocchiolo [3]

Affiliations + expand

PMID: 39232416 DOI: 10.1016/j.retram.2024.103464

Abstract

Background: While the detrimental role of donor-specific anti-HLA antibodies (DSAs) is well-described in the setting of hematopoietic stem cell transplantation (HSCT), few studies focus on non donor-specific ones and with controversial results.

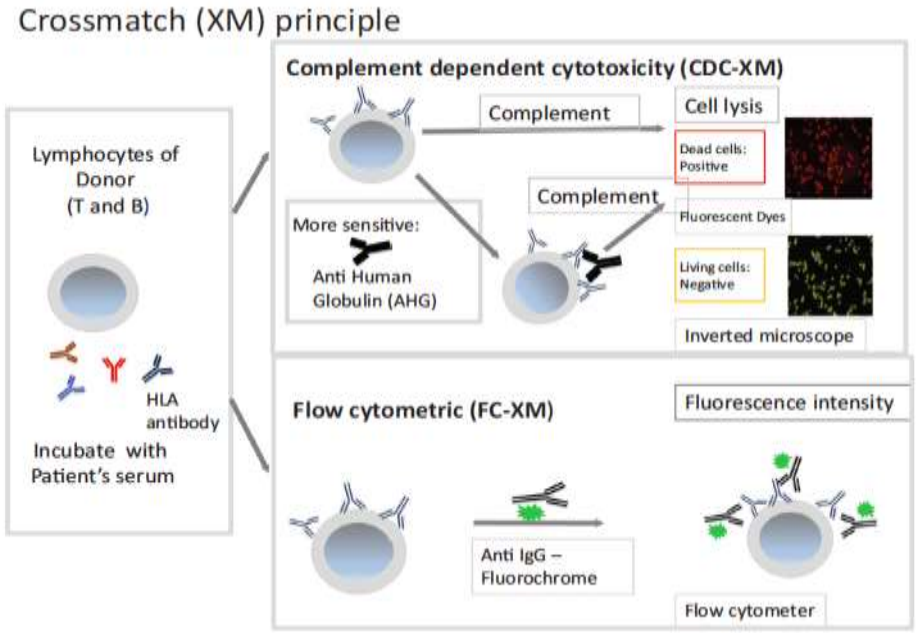
Methods: We here report our monocenter experience on 64 adult patients receiving allogeneic HSCT from a HLA-mismatched donor between 2014 and 2022 who were tested for the presence of anti-HLA antibodies before transplant, focusing on fifteen patients with non donor-specific anti-HLA antibodies.

Results: The survival of patients with non donor-specific anti-HLA antibodies was inferior with respect to patients without anti-HLA antibodies and similar to patients with DSAs. Median survival of patients with non donor-specific anti-HLA antibodies was 21 months (95 % CI: 9-42) vs. 61 months (95 % CI: 17-77) among the anti-HLA antibody-negative patients, with a significantly higher mortality incidence rate ratio (3.3 times-fold greater, p = 0.01). No pattern of death causes was found CONCLUSIONS: In this monocenter series of HLA-mismatched HSCTs, impaired survival was observed in adult patients having non donor-specific anti-HLA antibodies before transplant, similar to those with DSAs. Our findings support those antibodies as a negative predictive factor even if they are not directed against the donor, thus warranting further investigation on larger cohorts.

Keywords: Anti-HLA antibodies; HLA-mismatched; Hematopoietic stem cell transplantation; Survival.

DSA identification assays

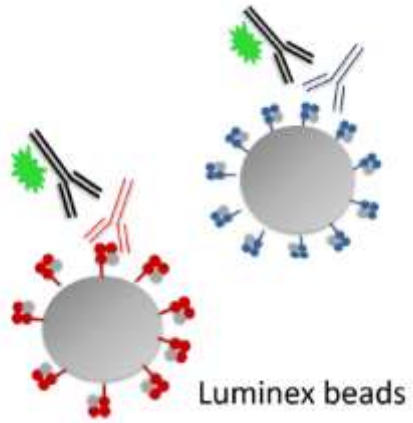
- **Cell-based:** require donor lymphocytes



- ✓ "Functional" test
- ✗ Low sensitivity

- ✓ Higher sensitivity
- ✗ Do not distinguish therapeutic antibodies (e.g. rituximab)

- **Solid-phase assays**: do NOT require donor lymphocytes



- ✓ High specificity and sensitivity
- ✓ Semiquantitative (MFI)>>>Virtual crossmatch
- ✓ Precise detection of anti-HLA antibodies
- ✗ Possible false positive or antibody levels underestimation
- ✗ No info about antibody functionality
- ✗ Not completely quantitative (MFI values do not translate directly into the antibody level)

- C1q assay ✓ distinguish complement fixing from non-complement fixing antibodies

M.P. Bettinotti, Human immunology 2022

Donor Specific Antibodies (DSA)

Highest relevance in partially HLA-mismatched allogeneic hematopoietic stem cell transplantation (multiple class I and II mismatches)[1]

Donor type	HLA loci								
HLA identical sibling	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
Haploidentical related	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
MUD 8/8	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
MUD 10/10	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
MUD 12/12	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
CBU 6/6	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1
	A	C	B	DRB1	DRB3/4/5	DQA1	DQB1	DPA1	DPB1

Classic “10 out of 10” HLA-matched alloBMTs: HLA-A, -B, -C, DRB1, and DQB1

HLA-DPB1, DRB3, DRB4, and DRB5 are not necessarily matched

Mismatching amenable to DSA formation occurs in more than half of the “10 out of 10” HLA-matched unrelated donor alloBMTs[2]

HLA antibodies are dynamic!

After inflammatory events, such as infection or tissue trauma, reactivation of dormant HLA-specific memory B cells may result in the production of DSAs without re-exposure to foreign tissue.[3]

Importance of HLA antibody reassessment over time.

[1] S.O. Ciurea et al, BMT 2018. [2] B.E. Shaw et al, Leukemia. 2010. [3] J.E. Locke et al, Am J Transplant. 2009.

Is there a DSA cutoff more detrimental to engraftment?

- **A positive test for DSA is considered when MFI is above 1,000** (the cutoff of MFI values used varies among transplant centers and laboratories).
- **The significance of low antibody levels remains unclear.** Rejection can occur at any DSA level for MFI>1000, the likelihood of developing PGF increases as the MFI levels increase.
  Low MFI levels (<3000) unlikely represent risk factors for transplantation.
  The incidence of PGF appears to increase with MFI levels above 5000.
- **There is no predictability by IgG mean fluorescence intensity (MFI) as to which of the antibodies will bind C1q because fixation is independent of antibody intensity.**
  Higher MFI levels (>5,000) correlate also with the complement-binding ability (which could contribute to a higher likelihood of rejection.
- **C1q testing is not done yet in many centers**: because of the high association with high DSA levels (>5,000 MFI), it should be presumed that high DSA levels are most likely complement-binding.
- **If C1q testing is positive or the pre-treatment DSA Luminex MFI is >20000, desensitization may not be successful.**

[1] S.O. Ciurea et al, BMT 2018. [2] D.E. Gladstone et al, Hematology Am Soc Hematol Educ Progr. 2017 [3] S. Bramanti et al, BBMT 2020

IMMUNOGENETICS

Recommendations

Histocompatibility assessment in hematopoietic stem cell transplantation: recommendations from the Italian Society for Immunogenetics and Transplantation Biology (Associazione Italiana di Immunogenetica e Biologia dei Trapianti - AIBT)

Roberto Crocchiolo[1], Caterina Fusco[2], Marco Andreani[3], Giovanni Rombolà[4], Michela Falco[5], Cinzia Vecchiato[6], Lucia Garbarino[7], Lia Mele[8], Allegra B. Mazzi[9], Alessandra Picardi[10,11], Letizia Lombardini[12], Simona Pollichieni[11], Maria C. De Stefano[13], Fabio Ciceri[11,13], Massimo Cardillo[13], Franco Papola[14]

These recommendations are intended for transplant programs performing the following types of HSCT:

- Transplantation from an HLA-identical or single-locus mismatched family donor.
- Transplantation from an HLA-haploidentical family donor.
- Transplantation from an unrelated donor.

These activities *must* be performed by internationally accredited laboratories (EFI, ASHI) and by personnel fulfilling the requirements of the accreditation bodies' standards **(1A)**.

Bone Marrow Transplantation
https://doi.org/10.1038/s41409-017-0062-8

REVIEW ARTICLE

Corrected: Correction

The European Society for Blood and Marrow Transplantation (EBMT) Consensus Guidelines for the Detection and Treatment of Donor-specific Anti-HLA Antibodies (DSA) in Haploidentical Hematopoietic Cell Transplantation

Stefan O. Ciurea[1] · Kai Cao[1] · Marcelo Fernandez-Vina[2] · Piyanuch Kongtim[3] · Monzr Al Malki[4] · Ephraim Fuchs[5] · Leo Luznik[5] · Xiao-Jun Huang[6] · Fabio Ciceri[7] · Franco Locatelli[8] · Franco Aversa[9] · Luca Castagna[10] · Andrea Bacigalupo[11] · Massimo Martelli[12] · Didier Blaise[13] · Rupert Handgretinger[14] · Denis-Claude Roy[15] · Paul O'Donnell[16] · Asad Bashey[17] · Hillard M. Lazarus[18] · Karen Ballen[19] · Bipin N. Savani[20] · Mohamad Mohty[21] · Arnon Nagler[22,23]

Kongtim P, et al. . ASTCT Consensus Recommendations on Testing and Treatment of Patients with Donor-specific Anti-HLA Antibodies. Transplant Cell Ther. 2024

Mismatched HLA class I molecules present a large repertoire of peptides (immunopeptidomes) which can be potential targets of T cell alloreactivity after allogeneic Hematopoietic Cell Transplantation. Therefore, the degree of immunopeptidome divergence between patient and donor HLA can affect the clinical outcome. Immunopeptidome divergence between HLA class I mismatches is here predicted by classifying HLA molecules into different groups based on their experimentally determined peptide binding motifs (PBM). Mismatches across PBM groups in the Graft versus Host (GvH) vector (Unidirectional GvH or Bidirectional) are predicted to be less well tolerated than mismatches within the same PBM group or in the Host versus Graft (HvG) vector (PBM matched or Unidirectional HvG). Alleles with no available data for PBM classification are indicated as PBM-unknown, and if in the mismatched locus, lead to exclusion from matching prediction.

Impact of the HLA Immunopeptidome on Survival of Leukemia Patients After Unrelated Donor Transplantation

Pietro Crivello, PhD[1]; Esteban Arrieta-Bolaños, PhD[1,2]; Meilun He, MPH[3]; Tao Wang, PhD[4,5]; Stephanie Fingerson, MS[3]; Shahinaz M. Gadalla, MD, PhD[6]; Sophie Paczesny, MD, PhD[7]; Steven G.E. Marsh, PhD[8]; Stephanie J. Lee, MD, MPH[5,9]; Stephen R. Spellman, MBS[3]; Yung-Tsi Bolon, PhD[3]; and Katharina Fleischhauer, MD[1,2]

PURPOSE Immunopeptidome divergence between mismatched HLA-DP is a determinant of T-cell alloreactivity and clinical tolerability after fully HLA-A, -B, -C, -DRB1, -DQB1 matched unrelated donor hematopoietic cell transplantation (UD-HCT). Here, we tested this concept in HLA-A, -B, and -C disparities after single class I HLA-mismatched UD-HCT.

PATIENTS AND METHODS We studied 2,391 single class I HLA-mismatched and 14,426 fully HLA-matched UD-HCT performed between 2008 and 2018 for acute leukemia or myelodysplastic syndromes. Hierarchical clustering of experimentally determined peptide-binding motifs (PBM) was used as a proxy for immunopeptidome divergence of HLA-A, -B, or -C disparities, allowing us to classify 1,629/2,391 (68.1%) of the HLA-mismatched UD-HCT as PBM-matched or PBM-mismatched. Risks associated with PBM-matching status were assessed by Cox proportional hazards models, with overall survival (OS) as the primary end point.

RESULTS Relative to full matches, bidirectional or unidirectional PBM mismatches in graft-versus-host (GVH) direction (PBM-GVH mismatches, 60.7%) were associated with significantly lower OS (hazard ratio [HR], 1.48; $P < .0001$), while unidirectional PBM mismatches in host-versus-graft direction or PBM matches (PBM-GVH matches, 39.3%) were not (HR, 1.13; $P = .1017$). PBM-GVH mismatches also had significantly lower OS than PBM-GVH matches in direct comparison (HR, 1.32; $P = .0036$). The hazards for transplant-related mortality and acute and chronic graft-versus-host disease but not relapse increased stepwise from full HLA matches to single PBM-GVH matches, and single PBM-GVH mismatches. A webtool for PBM-matching of single class I HLA-mismatched donor-recipient pairs was developed.

CONCLUSION PBM-GVH mismatches inform mortality risks after single class I HLA-mismatched UD-HCT, suggesting that prospective consideration of directional PBM-matching status might improve outcome. These findings highlight immunopeptidome divergence between mismatched HLA as a driver of clinical tolerability in UD-HCT.

J Clin Oncol 41:2416-2427.

Impact of the HLA Immunopeptidome on Survival of Leukemia Patients After Unrelated Donor Transplantation

Pietro Crivello, PhD[1]; Esteban Arrieta-Bolaños, PhD[1,2]; Meilun He, MPH[3]; Tao Wang, PhD[4,5]; Stephanie Fingerson, MS[3]; Shahinaz M. Gadalla, MD, PhD[6]; Sophie Paczesny, MD, PhD[7]; Steven G.E. Marsh, PhD[8]; Stephanie J. Lee, MD, MPH[5,9]; Stephen R. Spellman, MBS[3]; Yung-Tsi Bolon, PhD[3]; and Katharina Fleischhauer, MD[1,2]

CONTEXT

Key Objective

This article investigates the role of immunopeptidome divergence between single mismatched HLA-A, -B, or -C allotypes for clinical outcome of unrelated hematopoietic cell transplantation.

Knowledge Generated

Single class I HLA mismatches between donor and recipient with high immunopeptidome divergence predicted by distinct peptide-binding motif (PBM) groups present in the recipient, but not in the donor (graft-versus-host direction), are associated with inferior survival than mismatches with low immunopeptidome divergence predicted by identical PBM groups in recipient and donor.

Relevance *(C.F. Craddock)*

Prospective selection of donors without HLA class I PBM mismatches in the graft-versus-host direction may improve survival probability after HLA-disparate hematopoietic cell transplantation, which is particularly relevant for patient populations heavily dependent on mismatched donors. Validation of these data that identify HLA-restricted immunopeptidome divergence as a potentially important new driver of clinically relevant T-cell alloreactivity in an independent patient cohort will be important.*

*Relevance section written by *JCO* Associate Editor Charles F. Craddock, MD.

J Clin Oncol. 2023 May 1;41(13):2416-2427.

ABSTRACT

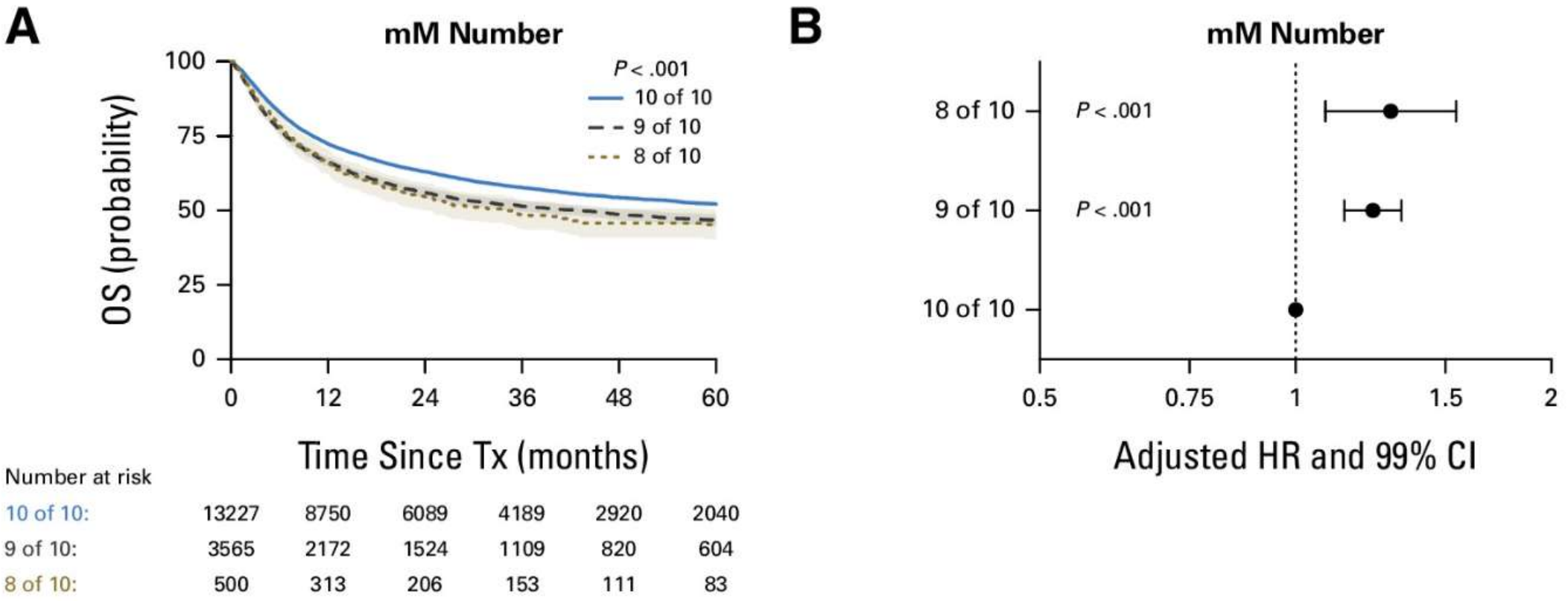
PURPOSE Human leukocyte antigen (HLA) mismatching can reduce survival of patients with blood cancer after hematopoietic cell transplantation (HCT). How recent advances in HCT practice, in particular graft-versus-host disease (GVHD) prophylaxis by post-transplantation cyclophosphamide (PTCy), influence HLA risk associations is unknown.

PATIENTS AND METHODS The study included 17,292 unrelated HCTs with 6-locus high-resolution HLA typing, performed mainly for acute leukemia or related myeloid neoplasms between 2016 and 2020, including 1,523 transplants with PTCy. HLA risk associations were evaluated by multivariable Cox regression models, with overall survival (OS) as primary end point.

RESULTS OS was lower in HLA mismatched compared with fully matched transplants (hazard ratio [HR], 1.23 [99% CI, 1.14 to 1.33]; $P < .001$). This was driven by class I HLA-A, HLA-B, HLA-C (HR, 1.29 [99% CI, 1.19 to 1.41]; $P < .001$) but not class II HLA-DRB1 and HLA-DQB1 (HR, 1.07 [99% CI, 0.93 to 1.23]; $P = .19$). Class I antigen-level mismatches were associated with worse OS than allele-level mismatches (HR, 1.36 [99% CI, 1.24 to 1.49]; $P < .001$), as were class I graft-versus-host peptide-binding motif (PBM) mismatches compared with matches (HR, 1.42 [99% CI, 1.28 to 1.59]; $P < .001$). The use of PTCy improved GVHD, relapse-free survival compared with conventional prophylaxis in HLA-matched transplants (HR, 0.77 [0.66 to 0.9]; $P < .001$). HLA mismatching increased mortality in PTCy transplants (HR, 1.32 [1.04 to 1.68]; $P = .003$) similarly as in non-PTCy transplants (interaction $P = .43$).

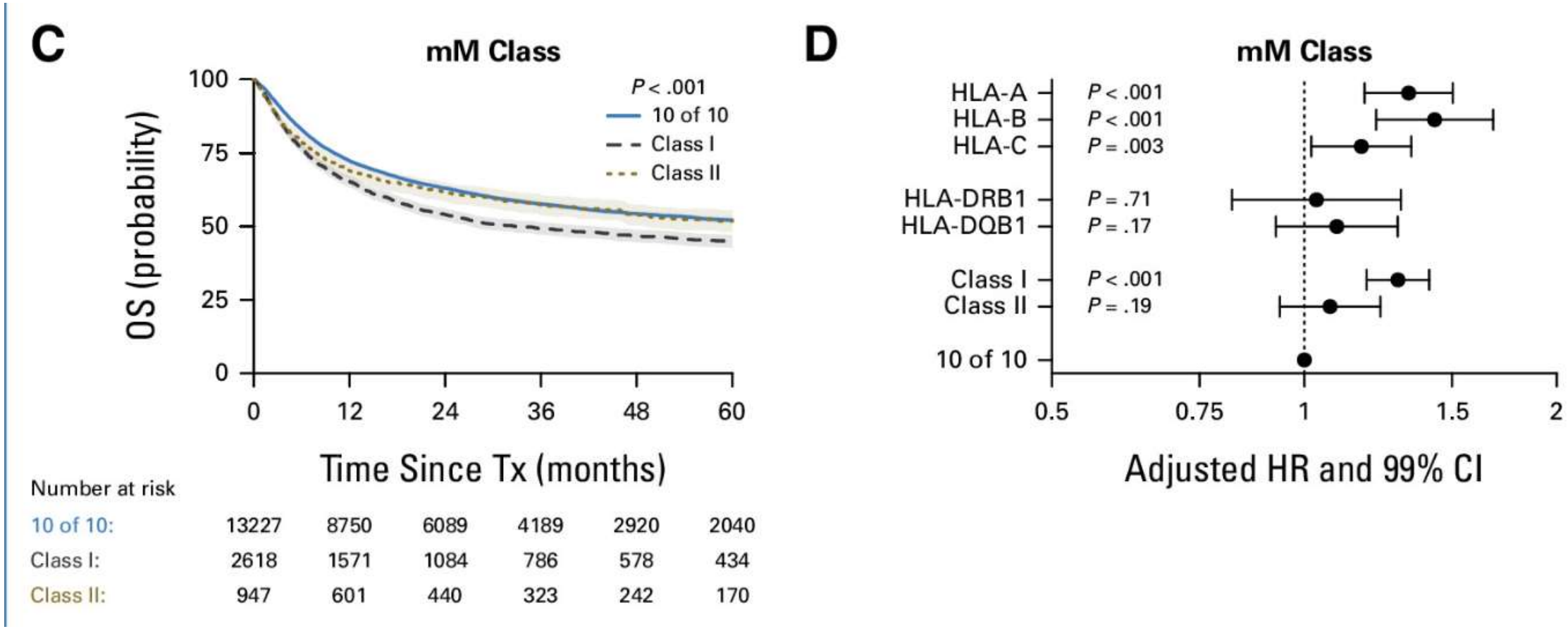
CONCLUSION Class I but not class II HLA mismatches, especially at the antigen and PBM level, are associated with inferior survival in contemporary unrelated HCT. These effects are not significantly different between non-PTCy compared with PTCy transplants. Optimized HLA matching should still be considered in modern HCT.

Arrieta-Bolaños E, et al. . J Clin Oncol. 2024 Oct;42(28):3287-3299.



Survival after contemporary HCT according to HLA mismatching. Kaplan-Meier and forest plots show overall survival (OS) probabilities (shaded areas) and adjusted HR estimates and their 99% CI for the entire cohort stratified according to (A, B) the number of mismatches (mM) at HLA-A, HLA-B, HLA-C, HLA-DRB1, or HLA-DQB1;

Arrieta-Bolaños E, et al. . J Clin Oncol. 2024 Oct;42(28):3287-3299.



Survival after contemporary HCT according to HLA mismatching. Kaplan-Meier and forest plots show overall survival (OS) probabilities (shaded areas) and adjusted HR estimates and their 99% CI for the entire cohort stratified according to (C, D) the specific mismatched HLA locus and class among the 9 of 10 pairs;

Arrieta-Bolaños E, et al. . J Clin Oncol. 2024 Oct;42(28):3287-3299.

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🔥 Nuovo software disponibile sul website AIBT!
Il "Class I HLA Peptide Binding Motif (PBM) Matching Tool" è un nuovo software utile per chi si occupa di Trapianto di midollo osseo.

🔬 Il software è stato sviluppato grazie ad una ricerca di CIBMTR® (Center for International Blood & Marrow Transplant Research®) e permette, inserendo i parametri immunogenetici dei potenziali donatori compatibili 9/10, di poter scegliere il donatore ottimale e che quindi dovrebbe garantire un risultato migliore post trapianto.

NK-mediated alloreactivity

Several studies have shown that the presence of an alloreactive NK population in the donor is associated with a better clinical course after haploidentical transplantation, as well as the presence of specific killer-cell immunoglobulin-like receptor (KIR) genotypes (B/X and B content value analysis) and certain activating KIR genes. These studies have led the European Society for Blood and Marrow Transplantation (EBMT) to include KIR gene analysis in their recommendations for haploidentical donor testing[8].

In cases where assessment of NK-mediated alloreactivity is required, the haploidentical recipient-donor pair *must* be evaluated at low resolution for the A locus and at high resolution for the HLA-B and -C loci **(1C)**. The donor's KIR gene pool study *should* also be performed **(2C)**.

Applications are available to detect the possibility of NK-mediated alloreactivity in the donor-recipient pair, such as the KIR ligand calculator software on the IPD-IMGT site. An in-depth study of NK-mediated alloreactivity in HSCT is reported in chapter "KIR gene repertoire analysis".

Crocchiolo R, et al. . Histocompatibility assessment in hematopoietic stem cell transplantation: recommendations from the Italian Society for Immunogenetics and Transplantation Biology (Associazione Italiana di Immunogenetica e Biologia dei Trapianti - AIBT). Blood Transfus. 2024

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GITMO

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L'associazione persegue esclusivamente finalità di solidarietà sociale, non ha fini di lucro ed ha come scopo lo sviluppo ed il progresso tecnologico dei trapianti di midollo osseo e di cellule staminali emopoietiche, da qualunque fonte esse provengano nonché lo sviluppo della base biologica.