

# Conditioning regimens for autologous transplant

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# Race against time



# Role of Conditioning in Autologous HCT

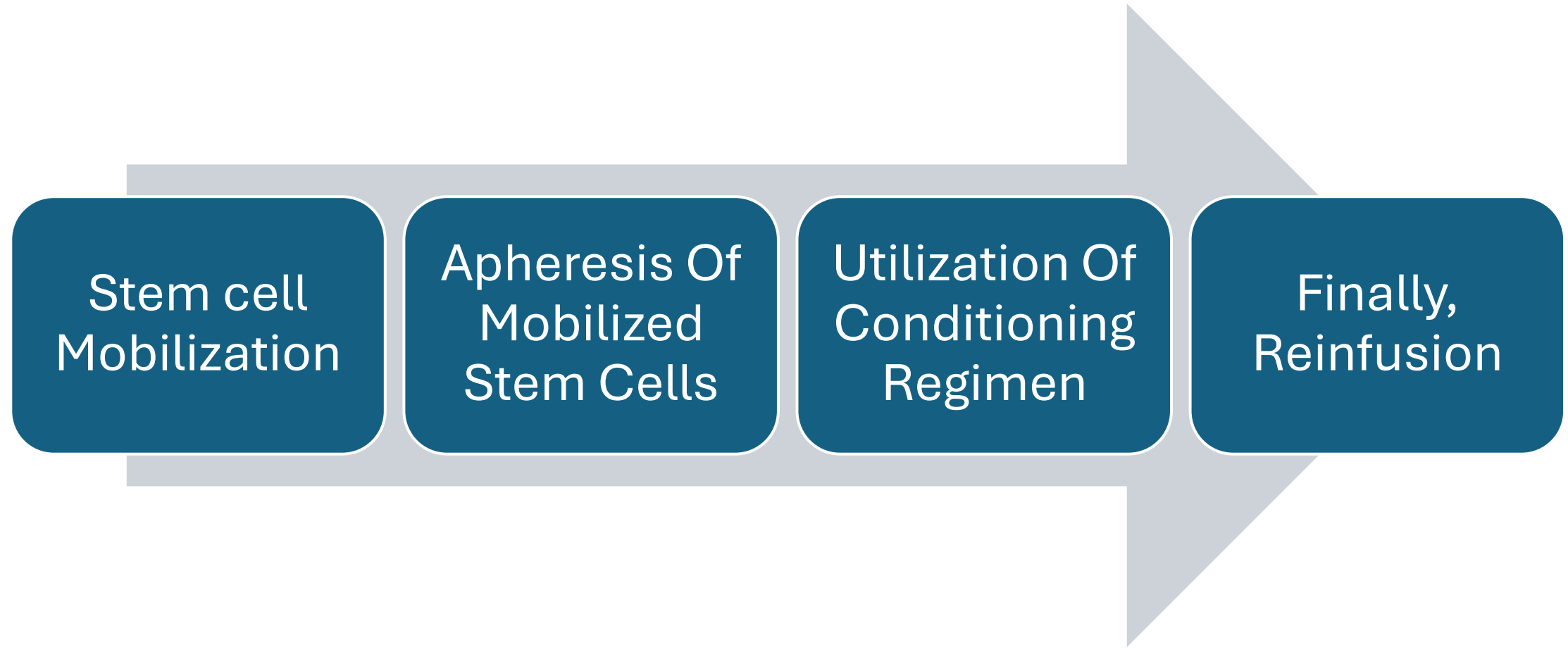
## Aims

- Deliver maximal cytoreduction
- Eradicate residual disease
- Create “space” in marrow
- Transient immunosuppression

## Constraints

- Heavily Pre-treated
- Older, comorbid patients
- Need to balance anti-tumor efficacy vs organ toxicity

# process of Auto-SCT



# Key Differences: Conditioning for Autologous vs Allogeneic SCT

Feature	Autologous SCT (ASCT)	Allogeneic SCT (Allo-SCT)
Primary goals of conditioning	<ul style="list-style-type: none"> <li>Maximal <b>tumour cytoreduction</b></li> <li>Create transient marrow aplasia to allow stem-cell rescue</li> </ul>	<ul style="list-style-type: none"> <li>Reduce tumour burden</li> <li><b>Immunosuppression for donor engraftment</b>, and enable <b>GvT</b> effect</li> </ul>
Immune effects	<b>no GvT</b>	Major part of efficacy is <b>GvT</b> ;
Intensity categories	Almost always <b>myeloablative</b>	<b>Myeloablative (MAC)</b> , <b>Reduced-intensity (RIC)</b> , <b>Non-myeloablative (NMA)</b>
Typical diseases	MM, NHL, HL, selected germ-cell tumours, some autoimmune diseases	AML, ALL, MDS/MPN, high-risk NHL/CLL, aplastic anaemia, Thal, SCD
Serotherapy	Not used	Frequently added
post-transplant immunosuppression	None	<b>Mandatory</b>
Early mortality (TRM)	Generally low -1–3%	Higher TRM-10 to 20%

# General Principles of Conditioning Regimen Selection

- **Patient-related factors**

- Age, frailty, renal/hepatic function, cardiac/pulmonary reserve

- **Disease-related factors**

- Diagnosis, disease status, risk cytogenetics, prior lines of therapy

- **Transplant-related factors**

- Stem cell source & dose, single vs tandem auto-HCT, planned consolidation/maintenance

- **Centre experience & logistics**

- Access to agents (BCNU, bendamustine, thiotepa), ICU support, infection burden, day-care vs in-patient models

**Goal:** maximize PFS/OS with acceptable NRM (<2–3% in MM, <5% in lymphoma)

**myeloma**



ELSEVIER

# Transplantation and Cellular Therapy

journal homepage: [www.tctjournal.org](http://www.tctjournal.org)



Review

## High dose (conditioning) regimens used prior to autologous stem cell transplantation in multiple myeloma

Mohammad O Ali<sup>1</sup>, Samer Al Hadidi<sup>2,\*</sup>

<sup>1</sup> Sanford School of Medicine, University of South Dakota, Sioux Falls, South Dakota

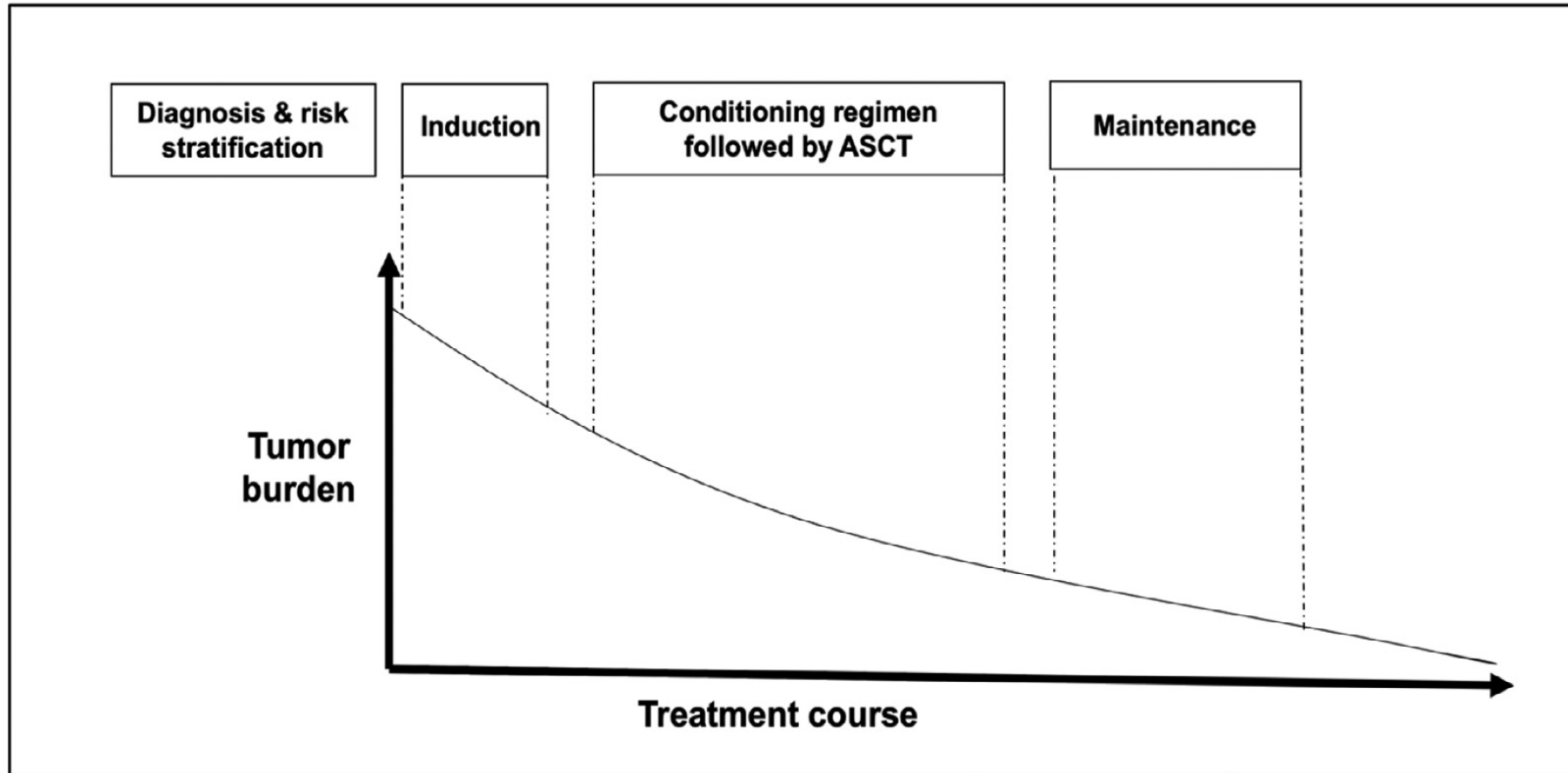
<sup>2</sup> Myeloma Center, Winthrop P. Rockefeller Cancer Institute, University of Arkansas for Medical Sciences, 4301 W. Markham St., #816, Little Rock, AR 72205, United States



# Myeloma

- Melphalan is an alkylating agent with broad antitumor activity, excellent ability to ablate the bone marrow
- HDM is defined as melphalan administered at a dose of 200 mg/m<sup>2</sup> or higher,
- Low-dose melphalan (LDM) is defined as melphalan administered at a dose of 70 to 180 mg/m<sup>2</sup>

# Treatment paradigm for transplant-eligible NDMM.



- Log-Kill Hypothesis — Skipper, Schabel & Wilcox Model
- A given dose of chemotherapy kills a constant *fraction* not a constant *number*, of tumor cells
- Most pronounced reduction in MM burden occur after starting a high-dose conditioning regimen

**How did mel 200 become the standard of care ??**



## Plenary paper

### Comparison of 200 mg/m<sup>2</sup> melphalan and 8 Gy total body irradiation plus 140 mg/m<sup>2</sup> melphalan as conditioning regimens for peripheral blood stem cell transplantation in patients with newly diagnosed multiple myeloma: final analysis of the Intergroupe Francophone du Myélome 9502 randomized trial

Philippe Moreau, Thierry Facon, Michel Attal, Cyrille Hulin, Mauricette Michallet, Frédéric Maloisel, Jean-Jacques Sotto, François Guilhot, Gérald Marit, Chantal Doyen, Jérôme Jaubert, Jean-Gabriel Fuzibet, Sylvie François, Lotfi Benboubker, Matthieu Monconduit, Laurent Voillat, Margaret Macro, Christian Berthou, Véronique Dorvaux, Bernard Pignon, Bernard Rio, Thomas Matthes, Philippe Casassus, Denis Caillot, Norbert Najman, Bernard Grosbois, Régis Bataille, and Jean-Luc Harousseau, for the Intergroupe Francophone du Myélome

- **IFM 9502** conditioning trial – the one that really nailed down **Mel200** as standard for MM auto-HCT.
  - patients younger than 65 years old
  - 8 Gy total body irradiation plus 140 mg/m<sup>2</sup> melphalan (arm A) versus
  - 200 mg/m<sup>2</sup> melphalan (arm B).
  - A total of 282 evaluable patients were compared—140 in arm A and 142 in arm B.

- 45-month survival was 65.8% in arm B versus 45.5% in arm A ( $P = .05$ ).

- Concluded that 200 mg/m<sup>2</sup> melphalan is less toxic and at least as effective conditioning regimen

- Mel 200 -standard of care before ASCT in multiple myeloma.

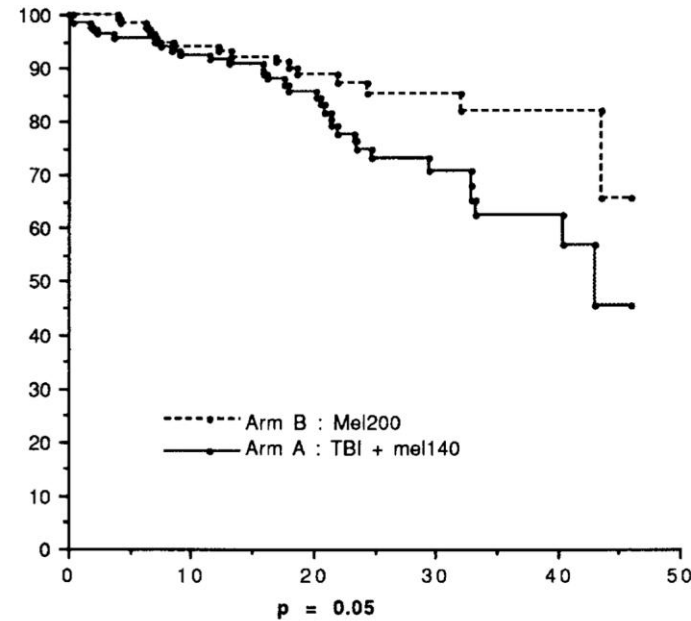


Figure 2. Survival according to treatment arm.

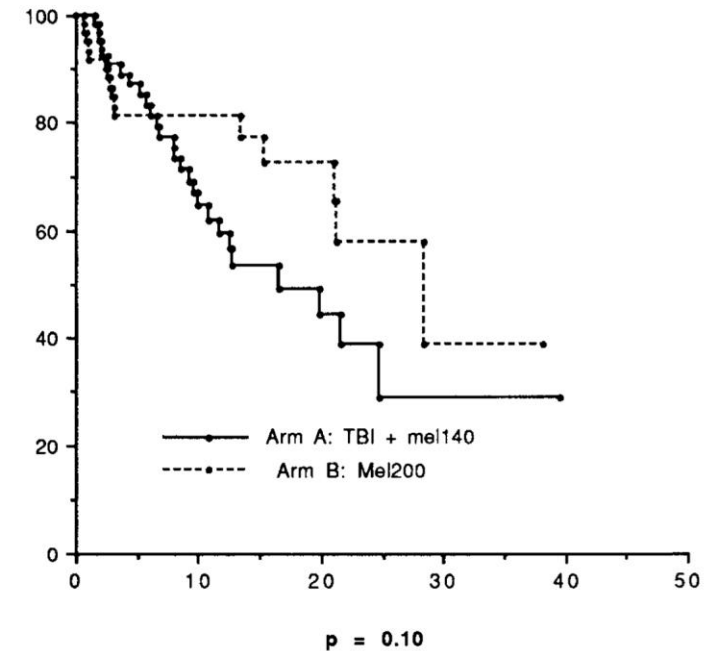


Figure 4. Survival after relapse according to treatment arm.

# Melphalan conditioning



- **MEL 280**

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Article | Published: 15 June 2018

# Final outcomes of escalated melphalan 280 mg/m<sup>2</sup> with amifostine cytoprotection followed autologous hematopoietic stem cell transplantation for multiple myeloma: high CR and VGPR rates do not translate into improved survival

[Parameswaran Hari](#), [Donna E. Reece](#), [Jasleen Randhawa](#), [Neal Flomenberg](#), [Dianna S. Howard](#), [Ashrof Z. Badros](#), [Aaron P. Rapoport](#), [Barry R. Meisenberg](#), [Joanne Filicko-Ohara](#), [Gordon L. Phillips](#) & [David H.](#)

Vesole 

# ESCALTED MEL 280



- Not superior to standard Mel200 historical controls.
- Median PFS  $\approx$  30–36 months range, essentially comparable to Mel200 era data.
- Melphalan has a steep toxicity curve; increasing dose adds more toxicity than tumor kill.
- Intensifying melphalan dose does not improve survival
- Mel200 remains the standard conditioning regimen for transplant-eligible MM.

# Beyond Melphalan Alone:MM

- **Mel + TBI**
  - higher toxicity, no consistent survival advantage
- **Busulfan–Melphalan (BuMel)**
  - Bu (often PK-guided) + Mel200 or lower; data suggest good disease control but higher mucosal/hepatic toxicity
- **Melphalan + Bortezomib**
  - Signal of deeper responses but added toxicity
- **Amyloidosis / POEMS**
  - Often dose-reduced Mel (100–140);
- **Real-world:** HD-Mel alone remains standard

# CONCLUSION AND FUTURE DIRECTIONS

- The current standard of care is melphalan at a dose of 200 mg/m<sup>2</sup> in young patients with normal renal function
- 140 mg/m<sup>2</sup> in older adults (65-70 years) and patients with renal insufficiency
- Combining melphalan with *busulfan*, *BENDA*, *BCNU*, and *novel agents such as bortezomib* may be beneficial, especially in patients with high-risk MM, but results need to be validated in large multicentre randomized clinical trials



**Move to**

**Lymphoma**

# Lymphomas

- Auto-HCT used in:
  - **Hodgkin lymphoma** – relapsed/refractory chemosensitive disease
  - **DLBCL/PMBCL** –second CR/PR; - individualized vs CAR-T
  - **Mantle cell lymphoma (MCL)** – consolidation in 1st CR with high-dose therapy
  - **Peripheral T-cell lymphomas (PTCL)** – consolidation in CR1 or salvage in selected cases

# Why BEAM became the standard

## Benefits:

- Most widely studied
- Best OS/PFS compared to CBV, BuCy, TBI in many series
- Fast hematopoietic recovery
- Lower TRM

## Limitations:

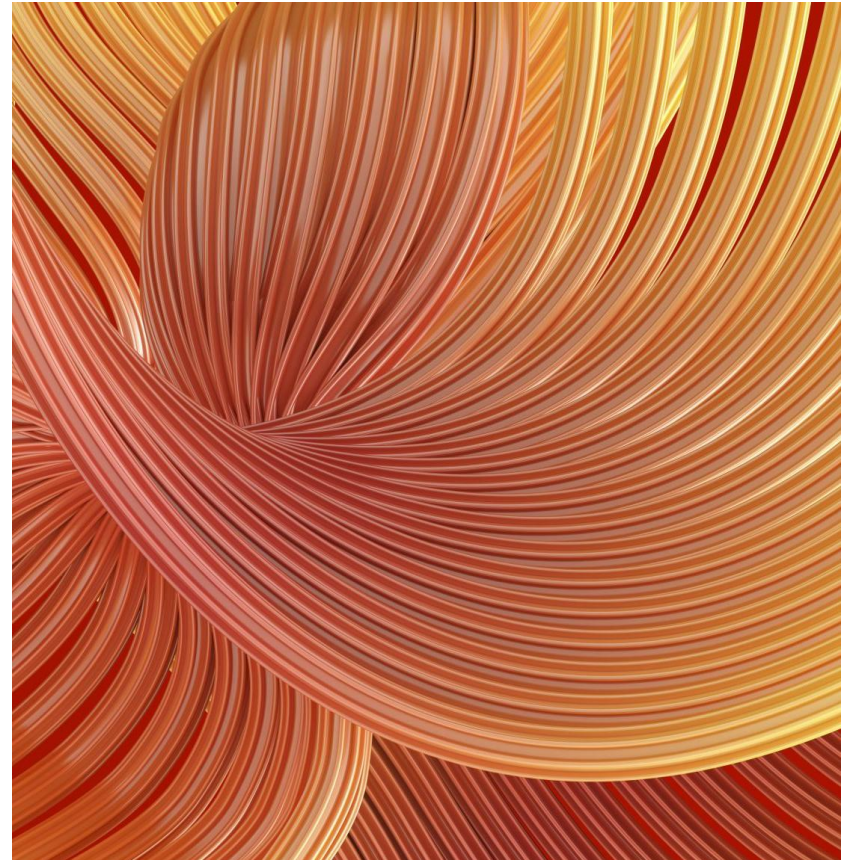
- BCNU pulmonary toxicity (16–64%)
- BCNU shortages
- Access issues in many countries

# Lymphoma CONDITIONING

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BEAM  
SUBSTITUTES

BETTER THAN  
BEAM





# Biology of Blood and Marrow Transplantation

journal homepage: [www.bbmt.org](http://www.bbmt.org)



Autologous Biol Blood Marrow Transplant 24 (2018) 1814–1822

## A Comparison of the Conditioning Regimens BEAM and FEAM for Autologous Hematopoietic Stem Cell Transplantation in Lymphoma: An Observational Study on 1038 Patients From Fondazione Italiana Linfomi



Jacopo Olivieri <sup>1,2,\*</sup>, Federico Mosna <sup>3</sup>, Matteo Pelosini <sup>4</sup>, Angelo Fama <sup>5</sup>, Sara Rattotti <sup>6</sup>, Margherita Giannoccaro <sup>7</sup>, Giuseppe Carli <sup>8</sup>, Maria Chiara Tisi <sup>8</sup>, Simone Ferrero <sup>9</sup>, Nicola Sgherza <sup>10</sup>, Anna Maria Mazzone <sup>11</sup>, Dario Marino <sup>12</sup>, Teresa Calimeri <sup>13</sup>, Giacomo Loseto <sup>14</sup>, Francesco Saraceni <sup>15</sup>, Gabriella Tomei <sup>16</sup>, Simona Sica <sup>17</sup>, Giulia Perali <sup>1</sup>, Katia Codeluppi <sup>5</sup>, Atto Billio <sup>3</sup>, Attilio Olivieri <sup>18</sup>, Enrico Orciuolo <sup>4</sup>, Rossella Matera <sup>7</sup>, Piero Maria Stefani <sup>19</sup>, Carlo Borghero <sup>8</sup>, Paola Ghione <sup>9</sup>, Nicola Cascavilla <sup>10</sup>, Francesco Lanza <sup>15</sup>, Patrizia Chiusolo <sup>17</sup>, Silvia Finotto <sup>12</sup>, Irene Federici <sup>18</sup>, Filippo Gherlinzoni <sup>19</sup>, Riccardo Centurioni <sup>2</sup>, Renato Fanin <sup>20</sup>, Francesco Zaja <sup>20</sup> on behalf of the Fondazione Italiana Linfomi Postgraduate Master Course

# Study Design

- Multicenter retrospective cohort.
- 1038 patients (BEAM 607; FEAM 431) undergoing ASCT 2008–2015.
- Lymphoma types:
  - Aggressive NHL: 59%
  - Hodgkin lymphoma: 27%
  - Indolent NHL: 14%
- Primary endpoint:
  - Severe infectious events (grade  $\geq 3$ ) within 100 days.
- Secondary endpoints:
  - ORR at day 100, OS, PFS, relapse incidence (RI), non-relapse mortality (NRM), engraftment kinetics, mucositis and GI toxicity.

## GI and mucosal toxicity: FEAM worse

- Grade  $\geq 3$  oral mucositis:  
**BEAM 31% vs FEAM 44% (p<.001)**
- Grade  $\geq 3$  diarrhoea:  
**BEAM 21% vs FEAM 28% (p=.007)**
- Grade  $\geq 3$  N/V:  
**BEAM 12% vs FEAM 17% (p=.03)**

## Infectious complications: FEAM worse

- Overall grade  $\geq 3$  infections: similar
- But grade  $\geq 4$  infections:
  - **BEAM 5% vs FEAM 11% (p<.001)**
- **Gram-negative bacteremia doubled:**
  - Mean isolates/patient: **0.10 (BEAM) vs 0.19 (FEAM), p<.001**
- Fungal infections also increased

## Engraftment & supportive care

- Neutrophil engraftment: similar
- **Platelet engraftment delayed with FEAM (12 vs 13 days, p<.001)**
- **Higher need for parenteral nutrition**
- **Longer hospitalization (21 vs 23 days, p<.001)**

# Response & Survival Outcomes

## Response at Day 100

CR+PR:

**BEAM 91% vs FEAM 88%**

## 2-year survival

**Overall survival:**

- BEAM **84.1%**
- FEAM **83.7%**  
→ **No difference**

**Progression-free survival:**

- BEAM **71.9%**
- FEAM **68%**

## Other outcomes

**Relapse incidence (1 year)**

- Similar (18% vs 21%)

**Non-relapse mortality**

- Slightly higher with FEAM (3.8% vs 2.6%),

**Infectious mortality**

- **Significantly higher in FEAM:**  
Subhazard ratio: **1.99**  
(**p=0.04**)

# Conclusions

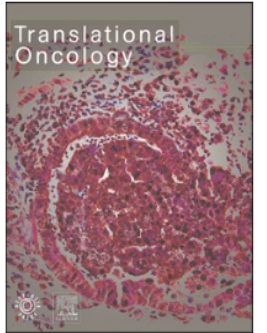
- Efficacy (OS/PFS): BEAM and FEAM are equivalent.
- **Toxicity:** FEAM is clearly more toxic—especially GI mucositis & Gram-negative sepsis.
- **Infectious mortality** is higher with FEAM.
- **Final conclusion:**  
**If BCNU is available, BEAM should remain the standard conditioning regimen for lymphoma ASCT.**




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## Translational Oncology

journal homepage: [www.elsevier.com/locate/tranon](http://www.elsevier.com/locate/tranon)

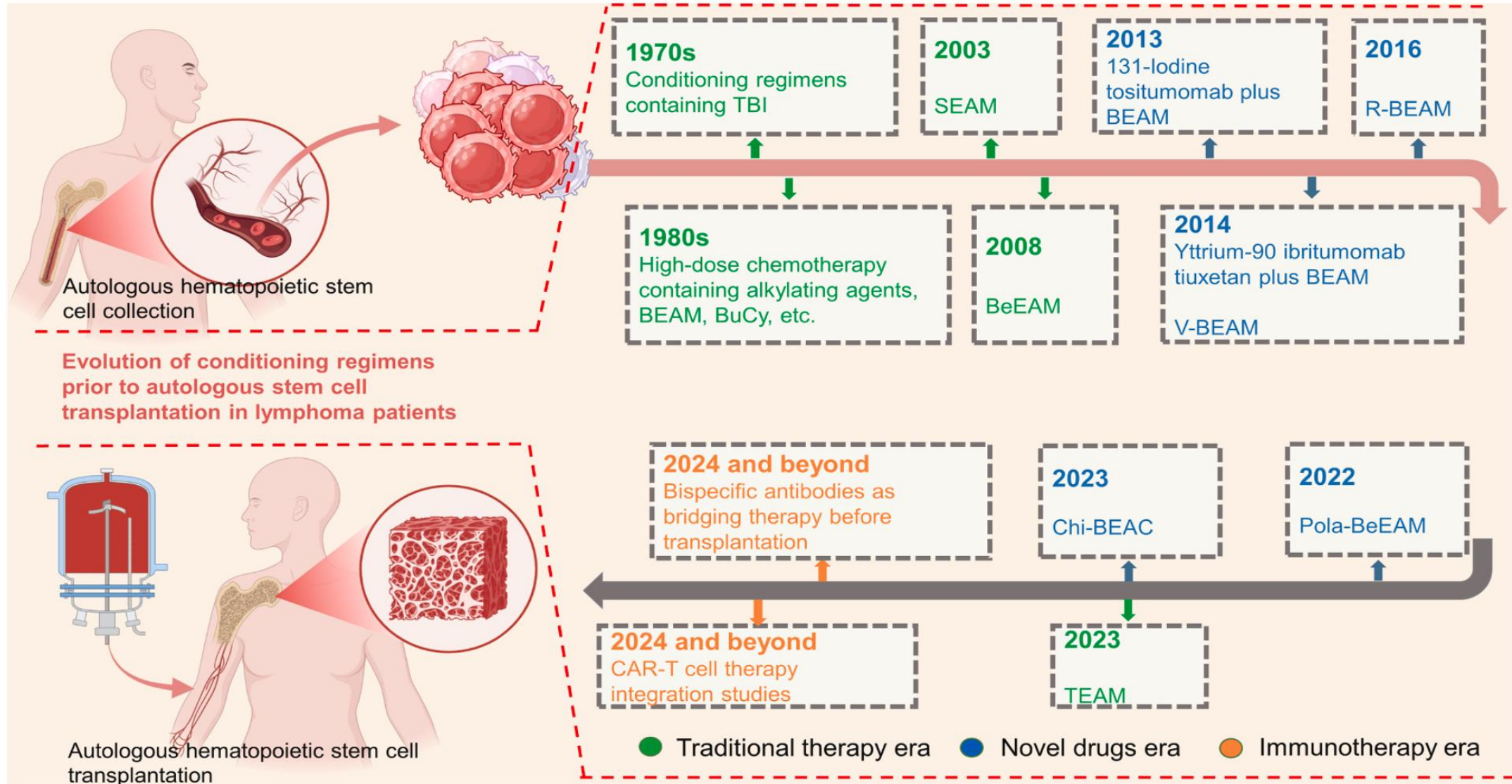


# Evolution of conditioning regimens prior to autologous stem cell transplantation in lymphoma patients

Hao Tian<sup>1</sup>, Ruiqi Wang<sup>1</sup>, Dan Cong, Yuansong Bai, Wenlong Zhang<sup>\*</sup> 

*Department of Hematology and Oncology, China-Japan Union Hospital of Jilin University, Changchun, 130033, China*

# Evolution of conditioning regimens FOR LYMPHOMA



# Classical Regimens

## BEAM (Gold Standard)

- Strongest evidence base; best OS/PFS in HL, DLBCL in multiple comparative studies.
- 3-year OS (HL): **79–95%**; PFS **62–92%**.
- 3-year OS (DLBCL): **58–61%**.
- Predictable engraftment (ANC ~11 days, PLT ~13.5 days).
- Main toxicity: **BCNU-related lung injury, mucositis.**

## CBV

Comparable efficacy in some FL and MCL subsets but **higher toxicity** (TRM 7–8%).  
Inferior to BEAM in HL and DLBCL in several studies.

## BuCy / BuCyE

- Similar survival to BEAM but **higher hepatotoxicity** (VOD 2–15%).
- Engraftment similar; more nausea/mucositis.

**Conclusion:** BEAM remains the most balanced classical regimen for lymphoma ASCT.

# Emerging “BEAM-Plus” & Novel-Agent Regimens

Radioimmunotherapy + BEAM

## Y-90 ibritumomab + BEAM:

- PFS ~69%, OS 91%
- Especially beneficial for early-relapse high-risk B-cell lymphoma.

## I-131 Tositumomab + BEAM

- 5-yr PFS 70%, OS 72%.
- Slightly higher mucositis with I-131.

# Targeted or Biologic Additions

## V-BEAM (bortezomib + BEAM):

- No survival advantage;
- ↑ neuropathy and GI toxicity

## R-BEAM (rituximab + BEAM):

- No improvement in OS/PFS
- Not recommended by CIBMTR.

## Pola-BeEAM (polatuzumab + BeEAM)

- Very high early PFS/OS (92%)
- Small, early-phase data → needs further validation.

## Chi-BEAC (chidamide + BEAC):

- Encouraging results in PTCL;
- Minimal TRM.

# Conclusions

- BEAM remains the cornerstone of conditioning for lymphoma ASCT due to its:
  - Strong long-term survival data
  - Acceptable toxicity
  - Predictable hematologic recovery
- Promising alternatives:
  - BeEAM, SEAM, GBC/GBM, thiotepa-based TEAM, especially in patients with pulmonary contraindications or BCNU inaccessibility.
  - Novel agents (pola-BEAM, RIT-BEAM) show potential but need RCTs.

# Other Alternatives to BEAM

# Bendamustine-based (BeEAM)

- Bendamustine replaces BCNU
- Excellent efficacy in MCL
- 3-yr PFS: 84% vs 63% in BEAM (significantly better)
- BUT: acute kidney injury (ARF 28–46%)
- Median recovery ~10 days

# Chidamide + BEAC (Chi-BEAC)

- Especially interesting in PTCL (including AITL)
- 2-yr PFS 81%, OS 86%
- Good tolerability

# Immunotherapy Era – Future Concepts

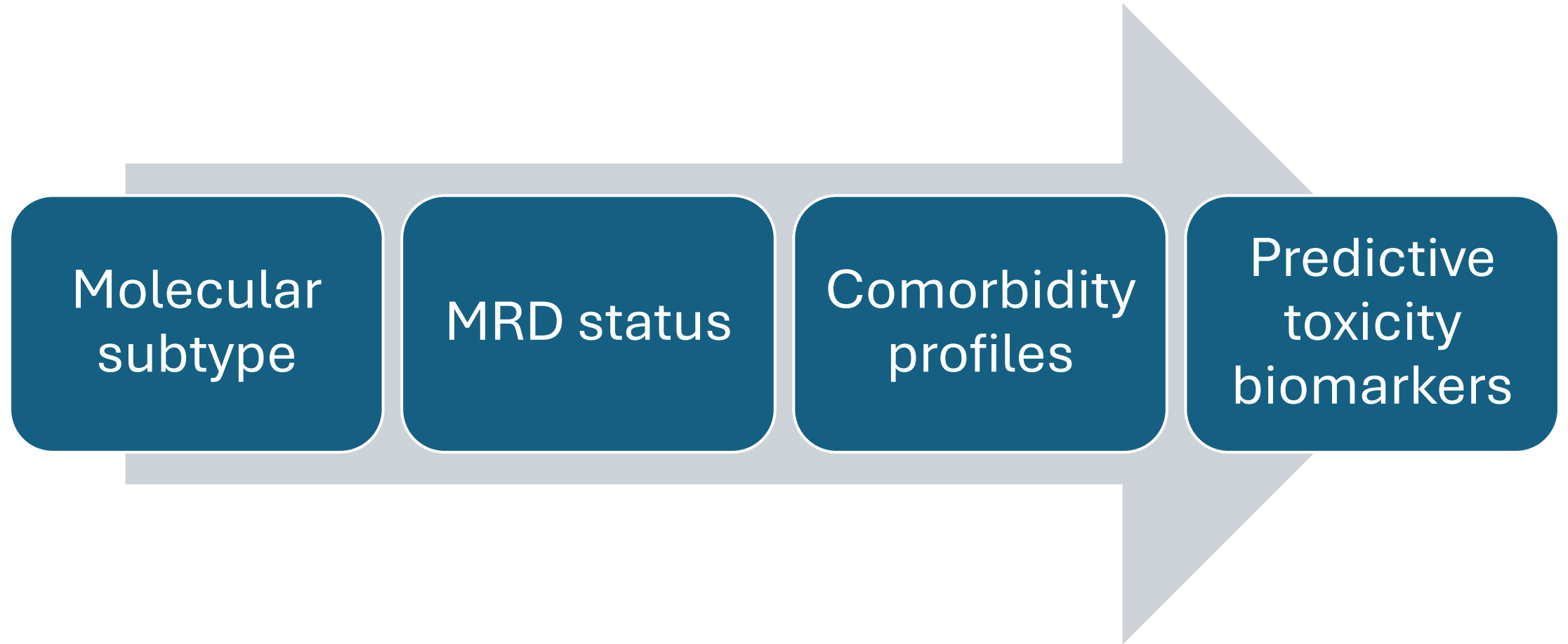
- Bispecific antibodies (e.g., glofitamab, epcoritamab)
  - Rapid debulking before stem cell mobilization
  - Potential synergy with high-dose therapy
  - But timing and CRS risk need definition

# BEAM as Gold Standard – But Not the Final Answer

Dimension	Why BEAM is the Gold Standard	Why We Need Better Than BEAM
Efficacy	<p><b>superior or at least best-in-class OS/PFS</b> for HL and DLBCL vs CBV, BuCy, TBI. E.g., 3-yr OS for HL and DLBCL with BEAM <math>\approx</math> <b>79% and 58%</b>,</p>	<p>Despite good results, <b>5-yr OS in aggressive lymphomas is often only ~50–60%</b>, and relapse remains the main cause of failure. BEAM does <b>not overcome high-risk biology</b></p>
Breadth of Activity	<p>Active across <b>HL, aggressive B-NHL, MCL, PTCL</b> – can be used as a “one-regimen-fits-most” backbone.</p>	<p>Lymphoma -heterogeneous; <b>one regimen is unlikely to be optimal</b> for all: CNS disease, heavily pretreated marrow, frail elderly, -We need <b>disease- and risk-adapted conditioning</b> rather than a single default.</p>
Hematopoietic Recovery	<p>Compared with other regimens, BEAM shows <b>faster neutrophil and platelet engraftment</b></p>	<p>Still causes <b>universal, profound pancytopenia</b> with high rates of febrile neutropenia;</p>
Organ Toxicity – Lungs (BCNU)	<p>BCNU gives strong anti-lymphoma effect and is a key reason for BEAM’s efficacy</p>	<p><b>Pulmonary toxicity is BEAM’s Achilles heel.</b> BCNU-based regimens have <b>16–64% pulmonary toxicity</b></p>
Logistics & Availability	<p>Entirely chemotherapy-based, no TBI logistics</p>	<p><b>BCNU supply problems</b> are increasingly common.</p>

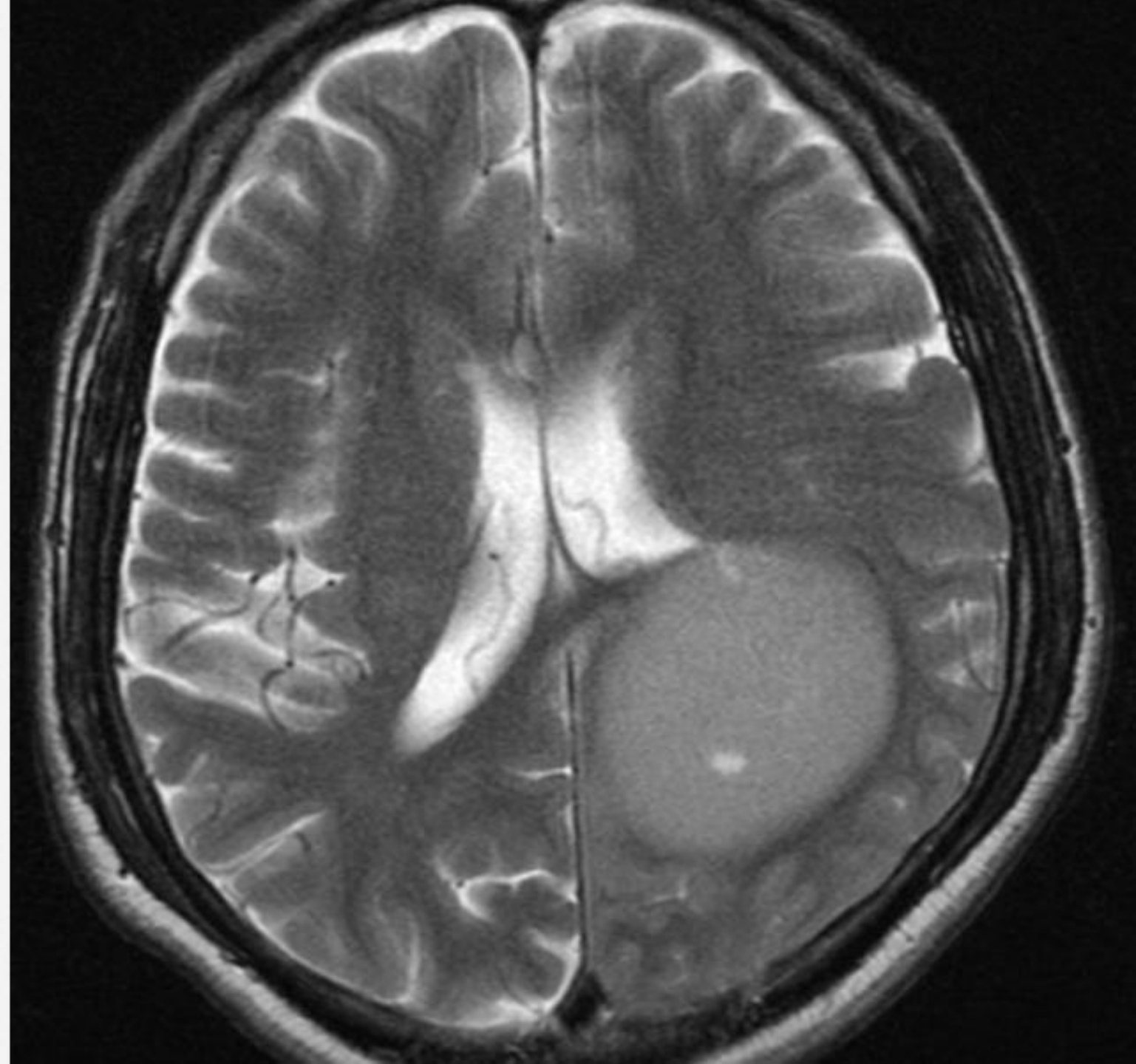
# LYMPHOMA -Future Paradigm:

Regimens will move toward precision, personalization, and integration of immunotherapy, guided by



ASCT IN  
PCNSL/CNS  
LYMPHOMA

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# Where Does Conditioning + ASCT Fit in PCNSL/CNS Lymphoma?

- Induction: high-dose methotrexate (HD-MTX)–based polychemotherapy
- Consolidation: either
  - Whole-brain radiotherapy (WBRT), or
  - HDC + autologous SCT (ASCT) – increasingly preferred to avoid neurocognitive decline.



## Review Article

# The role of autologous stem cell transplantation in primary central nervous system lymphoma

Andrés J. M. Ferreri<sup>1</sup> and Gerald Illerhaus<sup>2</sup>

<sup>1</sup>Unit of Lymphoid Malignancies, Division of Onco-Hematological Medicine, Department of Onco-Hematology, Istituto di Ricovero e Cura a Carattere Scientifico San Raffaele Scientific Institute, Milan, Italy; and <sup>2</sup>Klinik für Hämatologie, Onkologie und Palliativmedizin, Stuttgart Cancer Center, Tumorzentrum Eva Mayr-Stihl, Klinikum Stuttgart, Stuttgart, Germany

**Largest registry-based analyses** of ASCT outcomes in **Primary CNS Lymphoma (PCNSL)**

**CIBMTR (U.S.)** covering two decades (2000–2018).

# Study Design


- 350+ adult PCNSL patients undergoing ASCT were analyzed.
- Patients were grouped by age (<60 vs  $\geq$ 60 years) to understand the impact of age on ASCT outcomes.
- Evaluated endpoints:
  - Overall survival (OS)
  - Progression-free survival (PFS)
  - Non-relapse mortality (NRM)
  - Causes of death
  - Predictors of survival

# Key Findings

- ASCT is effective consolidation for PCNSL
  - 3-year OS and PFS after ASCT were favorable and consistent with European data.
- Majority of deaths were due to **disease relapse/progression**, not treatment-related mortality.

Article | Published: 13 May 2022

# Long-term efficacy, safety and neurotolerability of MATRix regimen followed by autologous transplant in primary CNS lymphoma: 7-year results of the IELSG32 randomized trial

[Andrés J. M. Ferreri](#) , [Kate Cwynarski](#), [Elisa Pulczynski](#), [Christopher P. Fox](#), [Elisabeth Schorb](#), [Claudia Celico](#), [Monica Falautano](#), [Alessandro Nonis](#), [Paul La Rosée](#), [Mascia Binder](#), [Alberto Fabbri](#), [Fiorella Ilariucci](#), [Mauro Krampera](#), [Alexander Roth](#), [Claire Hemmaway](#), [Peter W. Johnson](#), [Kim M. Linton](#), [Tobias Pukrop](#), [Jettes Sønderskov Gørløv](#), [Monica Balzarotti](#), [Georg Hess](#), [Ulrich Keller](#), [Stephan Stilgenbauer](#), [Jense Panse](#), [IELSG32 study investigators](#) [+ Show authors](#)

[Leukemia](#) **36**, 1870–1878 (2022) | [Cite this article](#)

**7444** Accesses | **140** Citations | **31** Altmetric | [Metrics](#)

# Key Long-term Results (7 years)

A. MATRix induction is superior

B. ASCT vs WBRT – both effective, but ASCT safer long-term

## 7-year PFS:

- ASCT ~50–55%
- WBRT ~45–50%  
(No significant difference)

## 7-year OS:

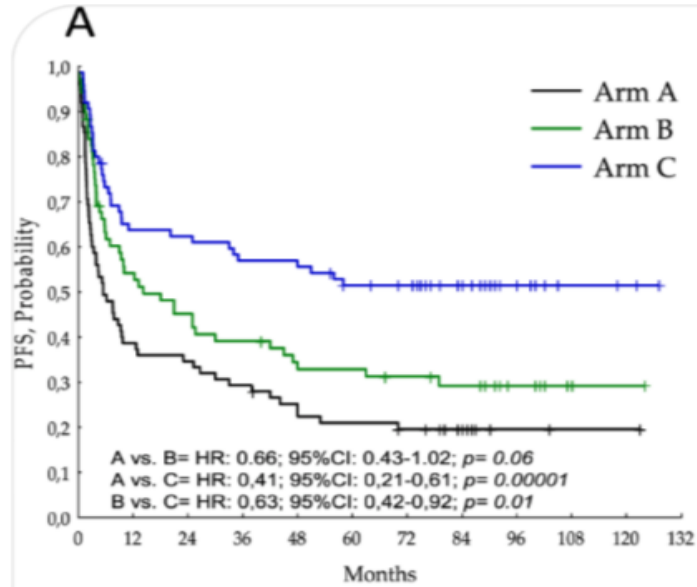
- ASCT ~60–70%
- WBRT ~55–65%

## Neurotoxicity:

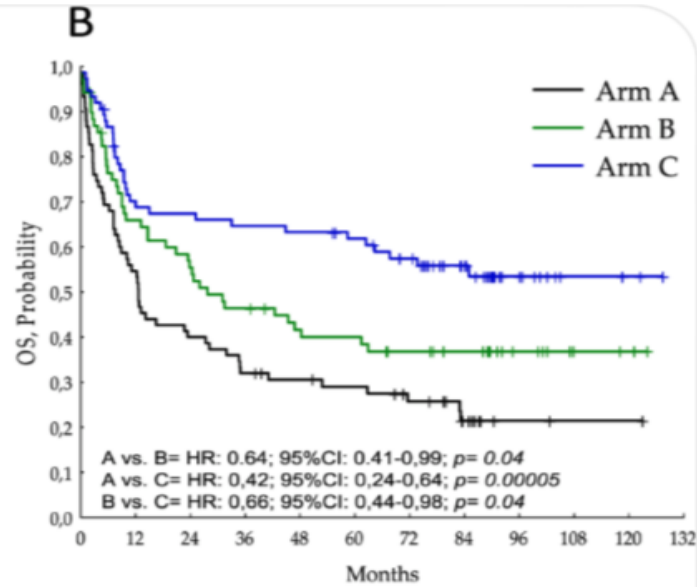
- WBRT associated with significant long-term neurocognitive decline
- ASCT associated with better preservation of cognition and quality of life

# IELSG32 7-YEAR RESULTS

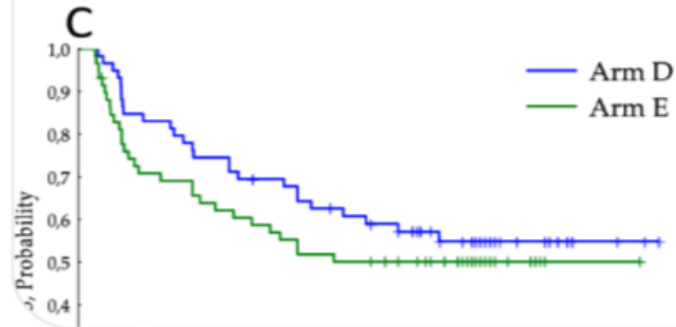
PFS BY INDUCTION ARM



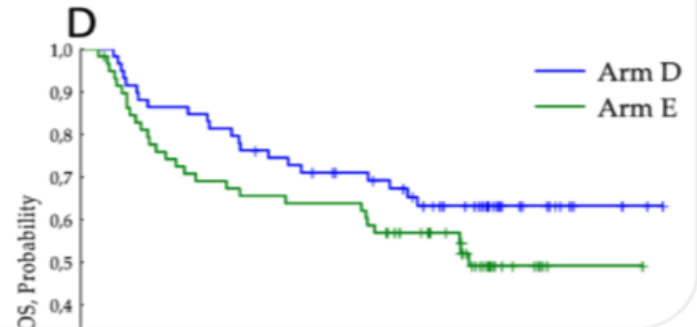
OS BY INDUCTION ARM



PFS BY CONSOLIDATION



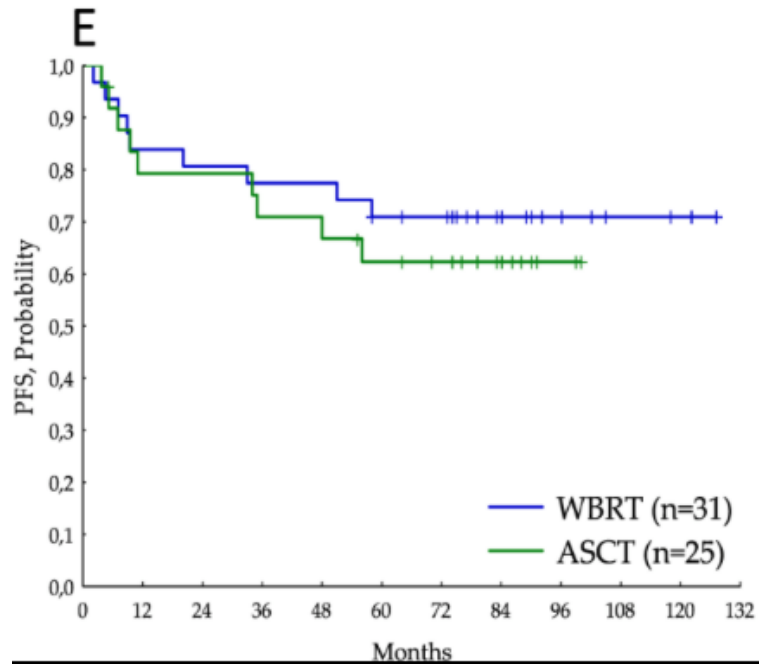
OS BY CONSOLIDATION



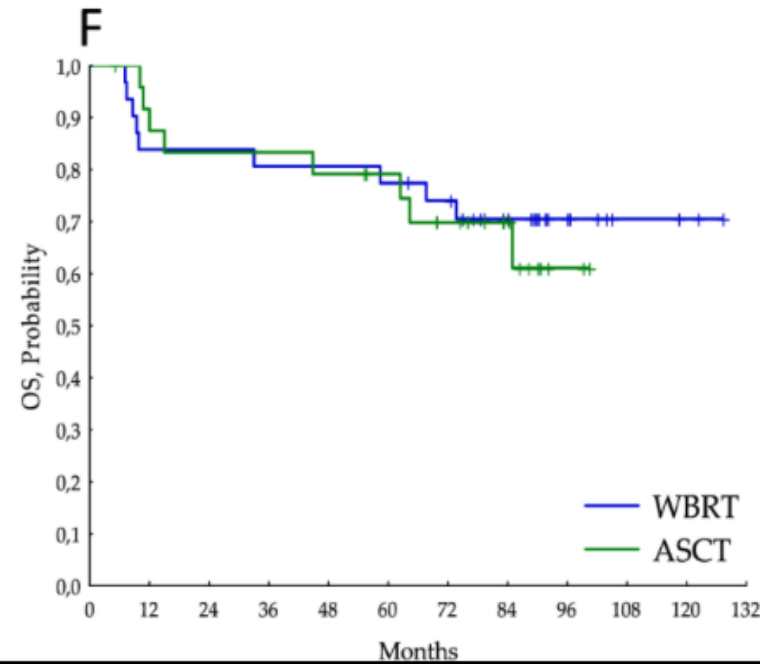
IELS G32 Arm	Treatment	Phase
Arm A	HD-MTX + Ara-C	Induction
Arm B	HD-MTX + Ara-C + Rituximab	Induction
Arm C	MATRix (MTX + Ara-C + Thiotepa + Rituximab)	Induction
Arm D	WBRT consolidation	Consolidation
Arm E	ASCT consolidation (thiotepa-based)	Consolidation

# IELSG32 7-YEAR RESULTS

NEUROCOGNITIVE OUTCOMES —  
OVERALL SCORE



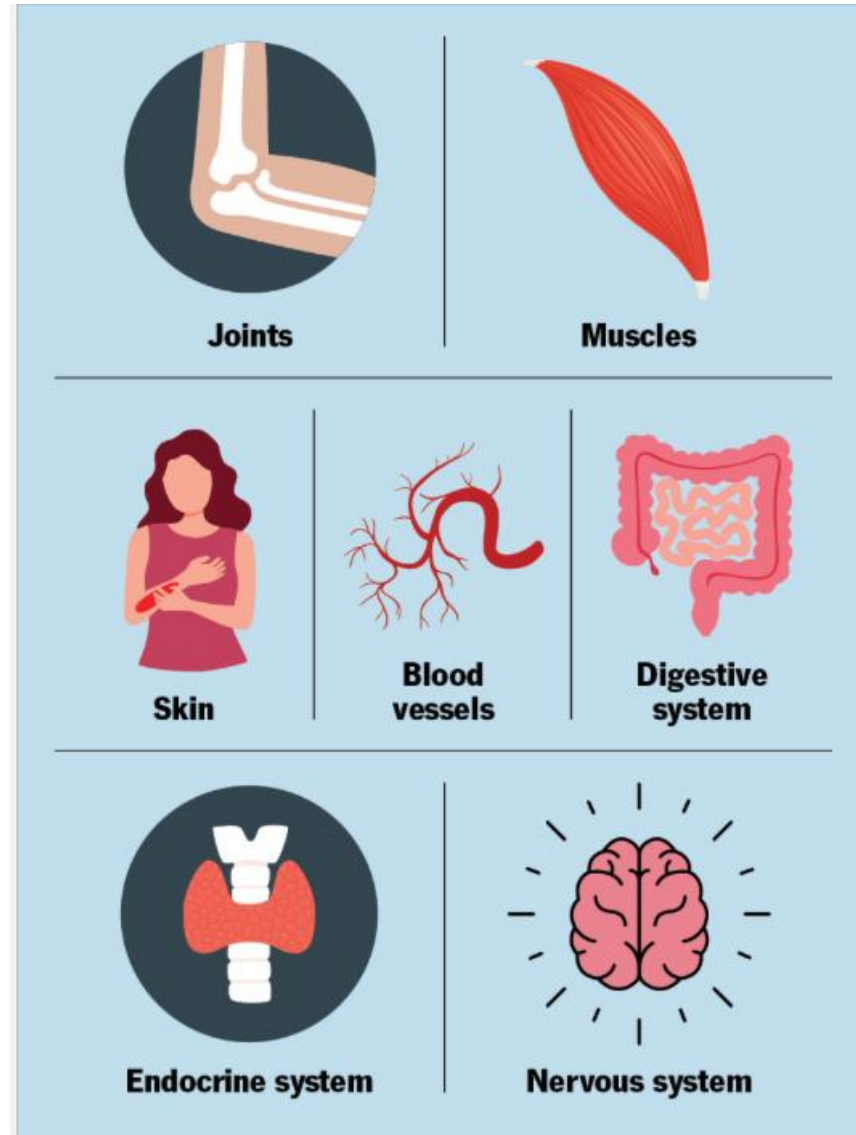
FUNCTIONAL/CNS TOXICITY  
DOMAINS



# Thiotepa based conditioning for PCNSL

- Thiotepa is highly lipophilic with excellent CSF and brain penetration, unlike BEAM, making it ideal for CNS disease.
- Allows potential cure without WBRT in many patients, reducing late neurotoxicity.
- Patients aged 60 or older had worse survival outcomes after thiotepa-based ASCT
- BEAM has limited CNS penetration

# ASCT in Autoimmune Disease



# Why ASCT in Autoimmune Disease?

- **Pathogenesis target**

- Autoimmune diseases - autoreactive immune repertoire (T and B cells, long-lived plasma cells, innate activation).

- **How ASCT works –**

- Conditioning (immunoablation): intermediate or high-dose chemo (e.g. cyclophosphamide + ATG / BEAM-like / Bu-based) → depletes autoreactive lymphocytes in blood, lymphoid tissues and inflamed organs
- Reinfusion of stem cells: “rescues” haematopoiesis, allowing rapid repopulation with new, more tolerant immune repertoire.

# Why ASCT in Autoimmune Disease?

## Immunological effects

- Profound resetting of T-cell compartments with reduction in effector/memory and expansion of naïve and Treg subsets
- Normalization of B-cell homeostasis and autoantibody decline in SSc, SLE and others

## Clinical goal

- Achieve long-term, drug-free remission
- Prevent irreversible organ damage
- Disease control even in patients who have failed conventional biologics/targeted therapies.

# Five most common autoimmune indications for auto-HSCT (ASCT)

- EBMT ADWP registry analyses ( $\approx 3,500$ – $4,600$  auto-HSCTs, 1996–2023)
  - Multiple sclerosis (MS)-By far the single most common indication.
  - Systemic sclerosis (SSc)
  - Crohn's disease
  - Systemic lupus erythematosus (SLE)
  - Rheumatoid arthritis / juvenile idiopathic arthritis (RA/JIA)

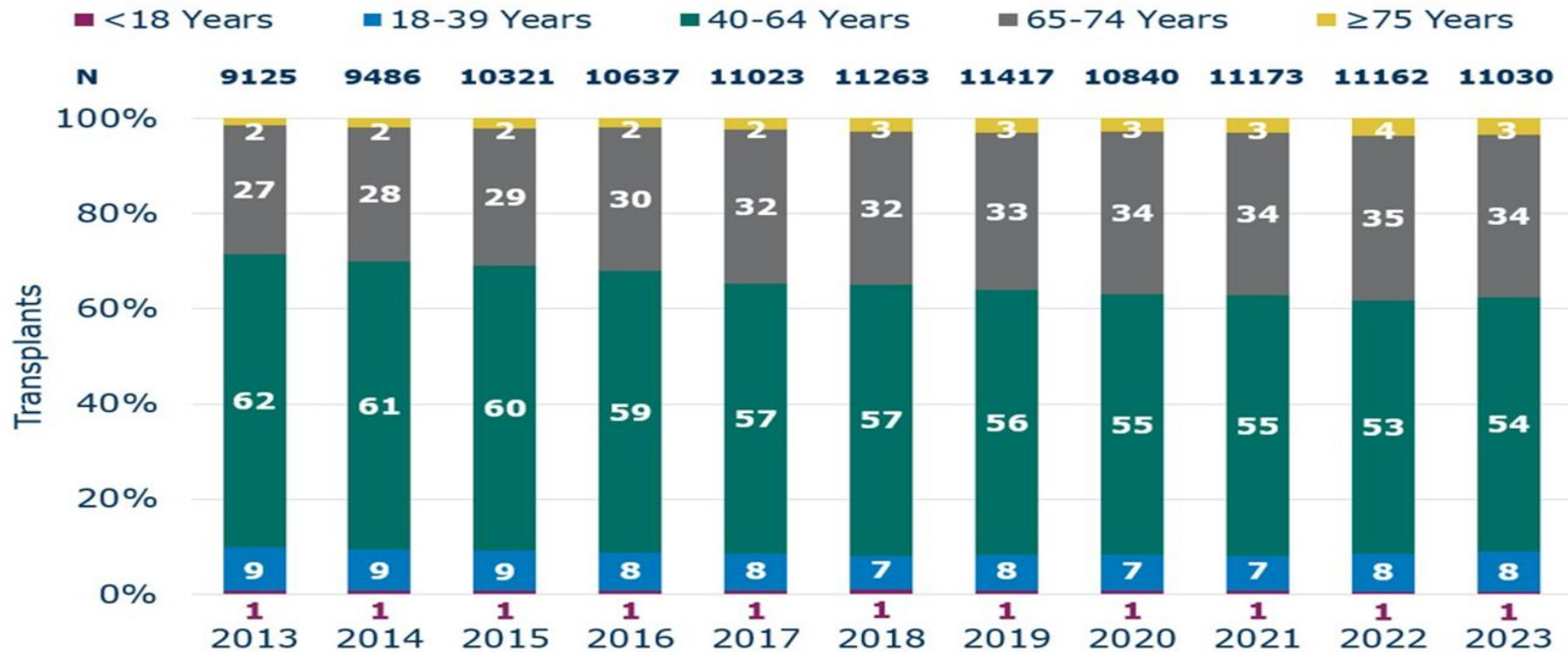
# Conditioning

- Across diseases, two regimens dominate:
  - Cyclophosphamide 200 mg/kg + ATG (Cy-ATG) and
  - BEAM-ATG
- Cy-ATG increasingly preferred for MS and rheumatologic disease because of similar efficacy and a better toxicity profile.

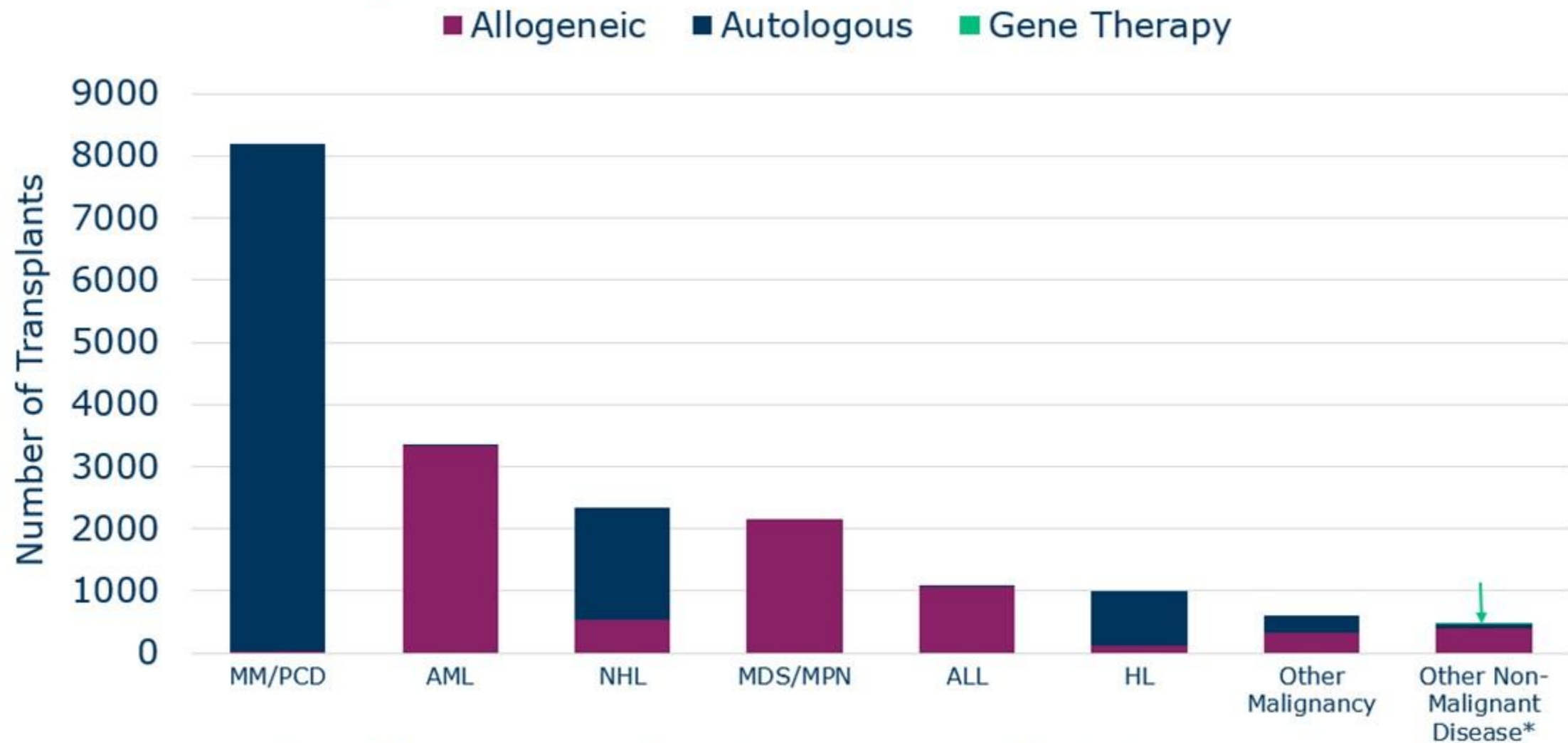
# CIBMTR TRENDS...

# Older age....

*Recipient Age of Autologous HCTs in the US*



## Number of HCTs by Indications in the US, 2023, Adult



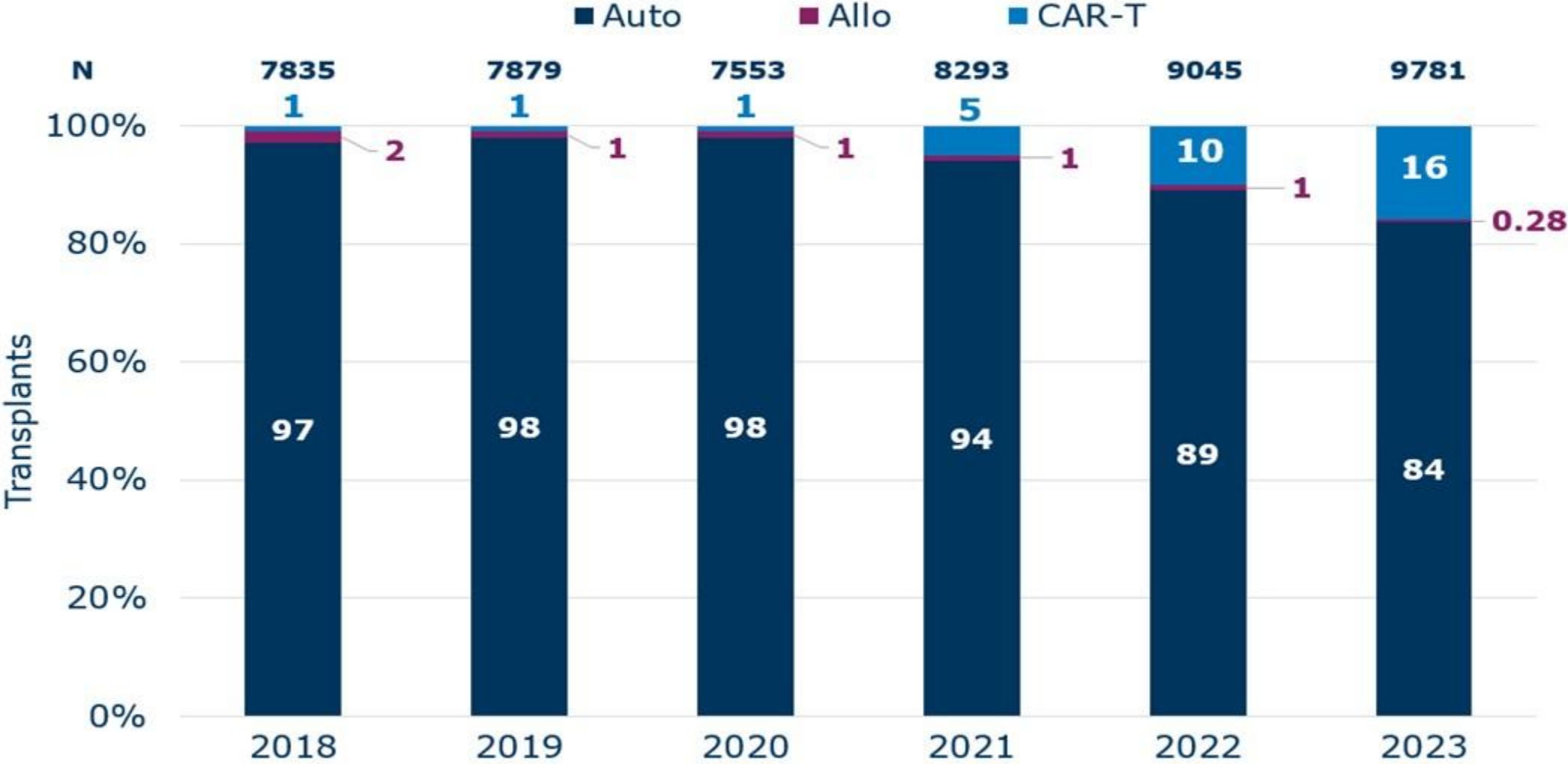
\*Includes 22 limited gene therapy events

Abbreviations:

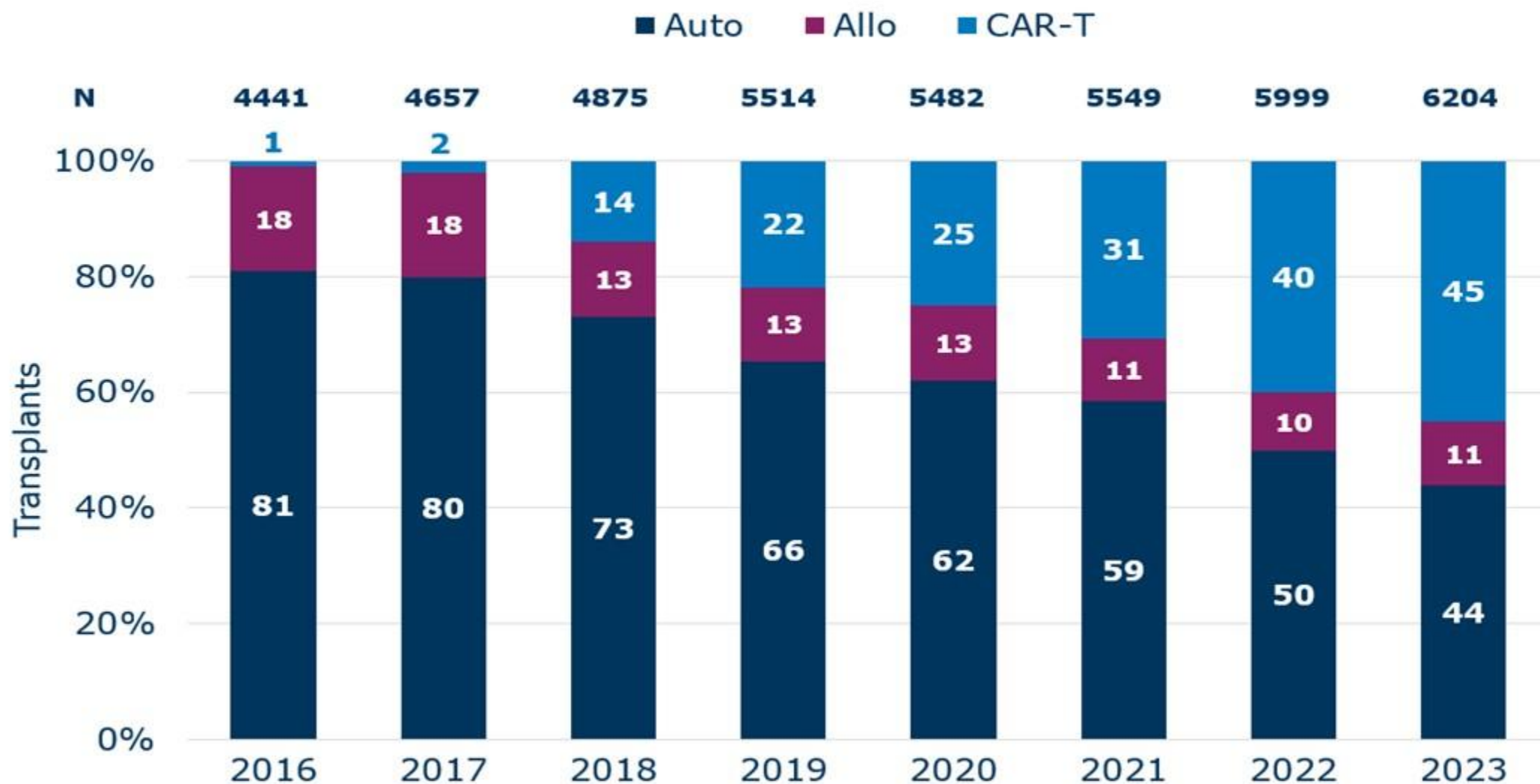
ALL, acute lymphoblastic leukemia;  
 AML, acute myeloid leukemia;  
 CLL, chronic lymphocytic leukemia;  
 HL, Hodgkin lymphoma;  
 MDS, myelodysplastic syndromes;

MM, multiple myeloma;  
 MPN, myeloproliferative neoplasms;  
 NHL, non-Hodgkin lymphoma;  
 PCD, plasma cell disorders.

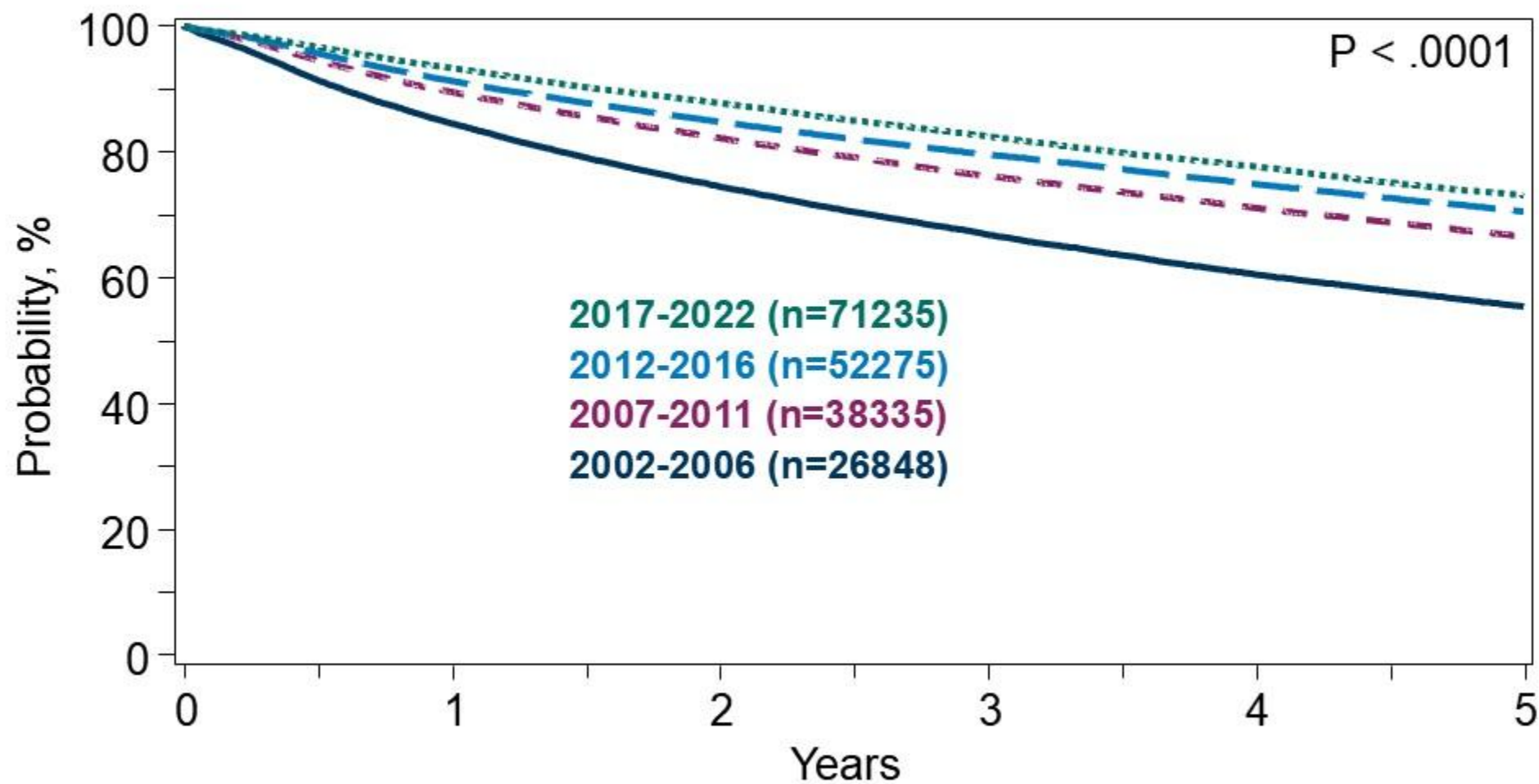
# Relative Proportion of Multiple Myeloma Treatment by Type in the US



## Relative Proportion of Lymphoma Treatment by Type in the US



## Trends in Survival after Autologous HCTs, in the US, 2002-2022



# Summarizing

- Conditioning therapy should Maximize cytoreduction & eradicate residual disease
- Balance efficacy vs toxicity in heavily pre-treated/older patients
- Melphalan 200 mg/m<sup>2</sup> = gold standard for MM
- BEAM remains standard for lymphoma ASCT
- Thiotepa-based conditioning (TEAM/TT-BU) preferred over WBRT in PCNSL
- Conditioning is moving toward personalized, disease-driven regimens incorporating targeted therapies and modern immunotherapy.

# QUESTION...

- **Which BEAM variant conditioning shows improved PFS in upfront mantle cell lymphoma, and what major toxicity increases with its use?**
  - A. BeEAM (bendamustine-EAM) – Increased renal toxicity (acute kidney injury)
  - B. LEAM (lomustine-EAM) – Increased pulmonary toxicity
  - C. FEAM (fotemustine-EAM) – Increased cardiac toxicity
  - D. CBV (cyclophosphamide-BCNU-etoposide) – Increased hepatic sinusoidal obstruction syndrome

# QUESTION...

- **Patient with diffuse large B-cell lymphoma (DLBCL) relapses within 6 months of completing first-line R-CHOP. What is the preferred next definitive treatment:**
  - A. Salvage chemotherapy followed by autologous stem cell transplantation (ASCT)
  - B. CAR-T cell therapy
  - C. Pola based therapy
  - D. Bispecific Antibody therapy

**Thank you for patient hearing**