
# Il trapianto allogenico oggi

**Patrizia Tosi**

**UO Ematologia Rimini**

CONCISE REPORT

# Bone Marrow Transplantation in Multiple Myeloma: Report From the European Cooperative Group for Bone Marrow Transplantation

By G. Gahrton, S. Tura, M. Flesch, A. Gratwohl, P. Gravett, G. Lucarelli, M. Michallet, J. Reiffers, O. Ringdén, M.T. van Lint, J.P. Vernant, and F.E. Zwaan

**Of 14 patients who received an allogeneic bone marrow graft from HLA-compatible sibling donors, 10 have survived for 6 to 34 months posttransplantation (median, 12 months). Four patients have died, two of relapse at extramedullary sites, one of severe acute GVHD, and one from GI bleeding and pericardial effusion. One patient is alive in relapse and four patients have signs of minimal persistent disease. Five patients are well without signs of active disease. Minor improvement in osteolytic lesions on X-ray were seen in three patients, but the X-ray bone structure was mainly unchanged in most patients. Bone marrow transplantation appears promising for treatment of certain patients with multiple myeloma.**

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**Table 1. Bone Marrow Transplantation in Multiple Myeloma**

| Patient | Sex/Age | Type of Myeloma | Treatment Before BMT | Time Diagnosis—BMT mo | Stage at BMT | Conditioning: Chemo | Conditioning: TBI Total Dose | Conditioning: TBI No. of Days | Survival mo post-BMT | GVHD: Acute Grade | GVHD: Chronic | Comments |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | F /29 | Plasma cell leukemia IgDλ | M, C+V+P+M+D | 7 | 2 | C 120 mg/kg CCNU 340 mg | 12.0 | 3 | 4½ | II | mild | Dead, meningeal relapse |
| 2 | F /45 | IgGκ | M+P+D+A | 18 | 1 | C 120 mg/kg M 140 mg/m² | 12.0 | 3 | 3½ | 0 | 0 | Dead, cerebral relapse |
| 3 | F /35 | IgAλ | C+P+CCNU+D | 7 | 1 | C 120 mg/kg | 10.0 | 1 | 12+ | 0 | 0 | Alive, well, minimal disease; persistent S-Ig <0.5 g/L; urinary light chains 0.2 g/L |
| 4 | M/35 | IgAκ | V+D+C+P | 6 | 2 | C 120 mg/kg BCNU 3.5 mg/kg V 2 mg,P60 mg/kg | 12.0 | 3 | 13½ | 0 | 0 | Alive, well minimal disease; persistent S-Ig 5g/L |
| 5 | F /39 | IgAλ | M+C+P | 13 | 1 | C 120 mg/kg M 140 mg/m² | 11.0 | 5 | 11+ | I | 0 | Alive, relapse |
| 6* | M/32 | BJκ | C+V+P+M | 25 | 3 | C 120 mg/kg | 10.0 | 1 | 9+ | I | 0 | Alive, well, no signs of active disease |
| 7* | F /38 | IgGλ | M+P | 18 | 3 | C 120 mg/kg | 10.0 | 1 | ½ | 0 | 0 | Dead, GI bleeding and pericardial effusion |
| 8* | F /46 | IgAκ | M+P | 5½ | 3 | C 120 mg/kg | 10.0 | 1 | 34+ | I | 0 | Alive, well, no signs of active disease |
| 9 | M/29 | BJκ | M+P | 8 | 3 | C 120 mg/kg | 10.0 | 3 | 12+ | I | 0 | Alive, well, no signs of active disease |
| 10 | M/44 | IgAλ | M+P | 8 | 1 | C 120 mg/kg M 4 mg/kg | 10.0 | 1 | 8+ | I | 0 | Alive, well, minimal disease 10% plasma cells in the bone marrow |
| 11* | F /35 | IgGκ | M+P | 24 | 1 | C 120 mg/kg | 10.5 | 1 | 28+ | I | mild | Alive, well, no signs of active disease |
| 12* | M/44 | IgAκ | M+P M+D+BCNU+C+V | 16 | 3 | C 120 mg/kg M 2 mg/kg BCNU 5.5 mg/kg | 9.5 | 1 | 12+ | I | mild | Alive, well, no signs of active disease |
| 13* | M/34 | IgAκ | M+P M+P+BCNU+C+V | 58 | 1 | C 120 mg/kg M 2 mg/kg BCNU 5.5 mg/kg | 10.0 | 1 | 2 | IV | 0 | Dead, severe acute GVHD |
| 14 | F /38 | IgGκ | V+C+M+P V+D+P | 14 | 1 | C 120 mg/kg | 12.0 | 3 | 6+ | I | mild | Alive and well, minimal disease; persistent S-Ig 6 g/L |

Abbreviations: M, melphalan; C, cyclophosphamide; V, vincristine; P, predniso(lo)ne (or dexamethasone); A, cytosine arabinoside (ARA-C); D, doxorubicin; CCNU, lomustine; BCNU, carmustine.

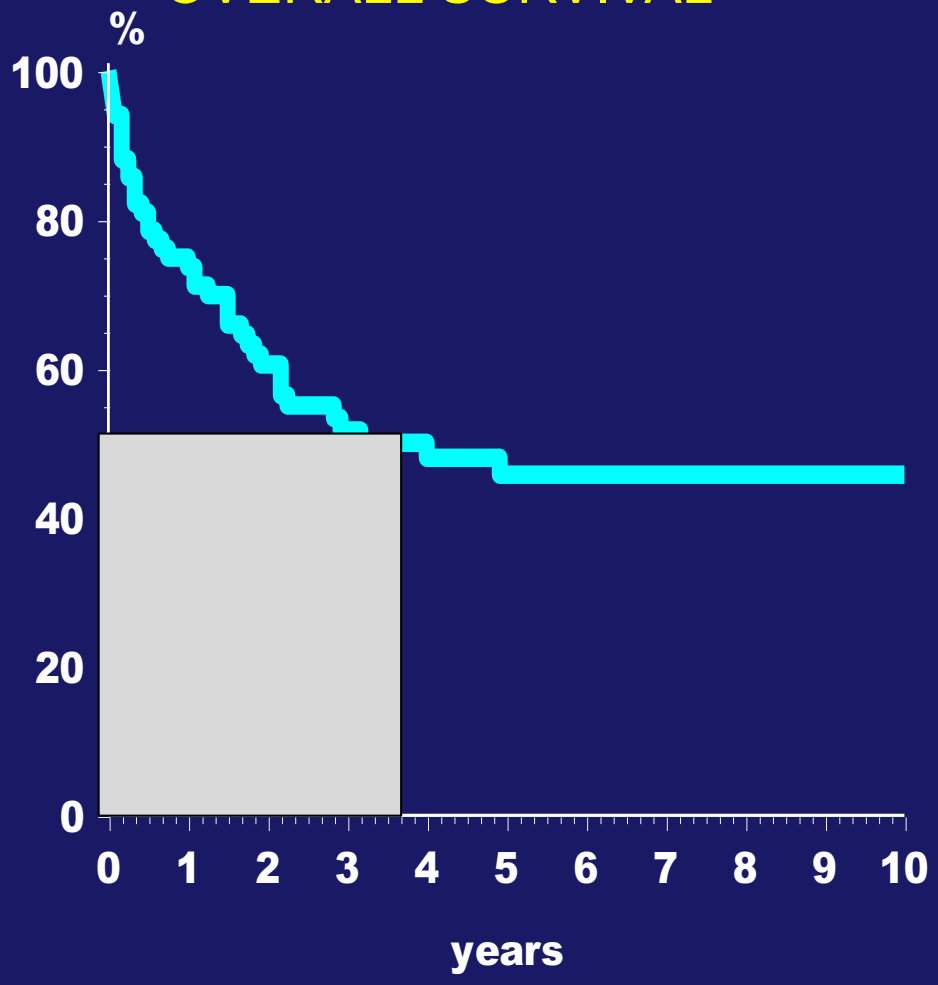
*Earlier reported after shorter follow-up time (5,6)

# MYELOABLATIVE SCT 1990-2003
## Bologna experience

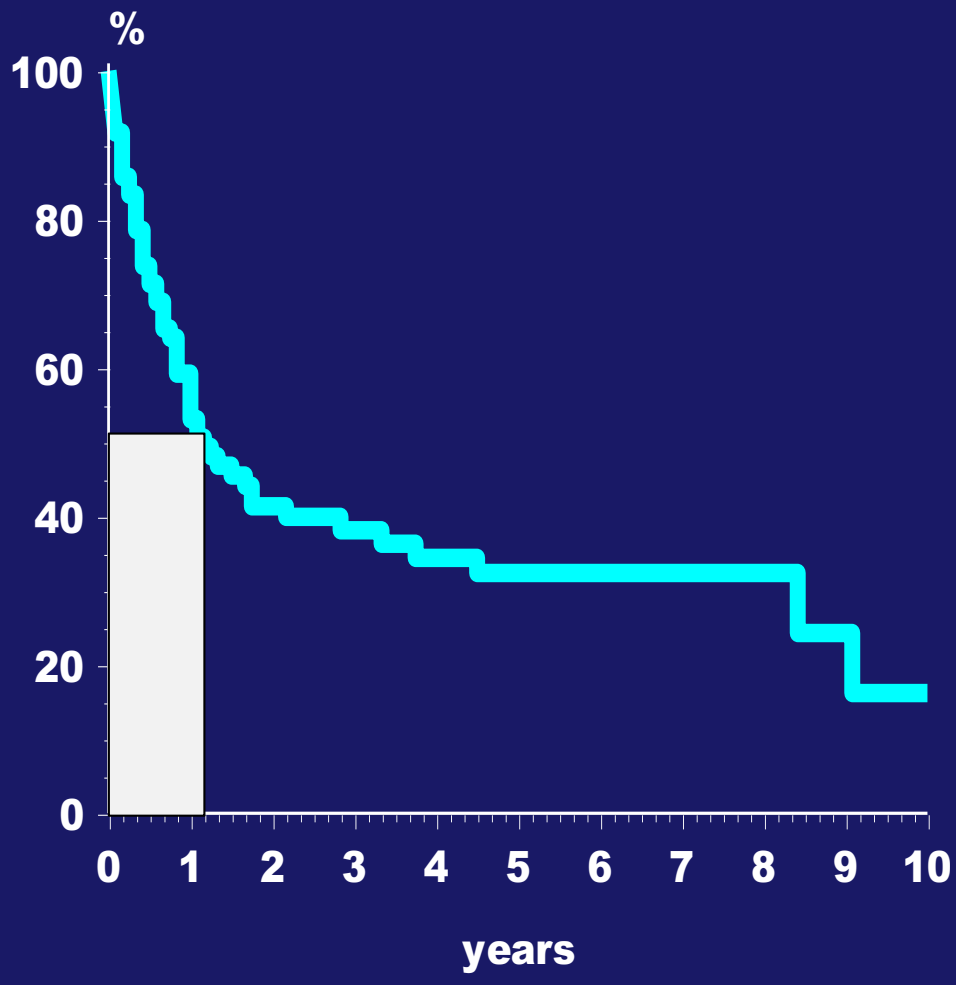
| | |
|---|---|
| **Study period** | **1990-2003** |
| **N° pts** | **84** |
| **Males:Females** | **48:36** |
| **Median age at Tx (range)** | **44 (21-55)** |
| **Median interval Dg-Tx (range)** | **17 (1-168)** |
| **Stage III at Tx (%)** | **56 (67)** |
| **Status at Tx** | |
| **Refractory (%)** | **47 (56)** |
| **Responsive (%)** | **37 (44)** |

# MYELOABLATIVE SCT 1990-2003
## Bologna experience

### OVERALL SURVIVAL




### EVENT-FREE SURVIVAL




Seràgnoli Institute -Bologna, Italy

# Melphalan-prednisone versus alternating combination VAD/MP or VND/MP as primary therapy for multiple myeloma: final analysis of a randomized clinical study

**Michele Cavo, Monica Benni, Sonia Ronconi, Mauro Fiacchini, Alessandro Gozzetti, Elena Zamagni, Claudia Cellini, Patrizia Tosi, Michele Baccarani, Sante Tura**
***Writing committee of the "Bologna 90" clinical trial***
Institute of Hematology and Medical Oncology "Seràgnoli", University of Bologna, Italy

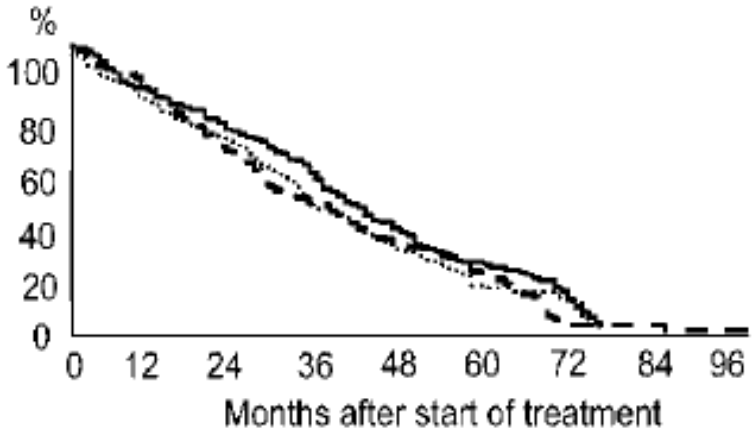



**Figure 1. Probability of survival for patients randomized to receive MP (—)or VAD/MP (- - -)or VND/MP (– – –) (*p*, not significant).**

**Table 2. Response to the three treatments of the study.**

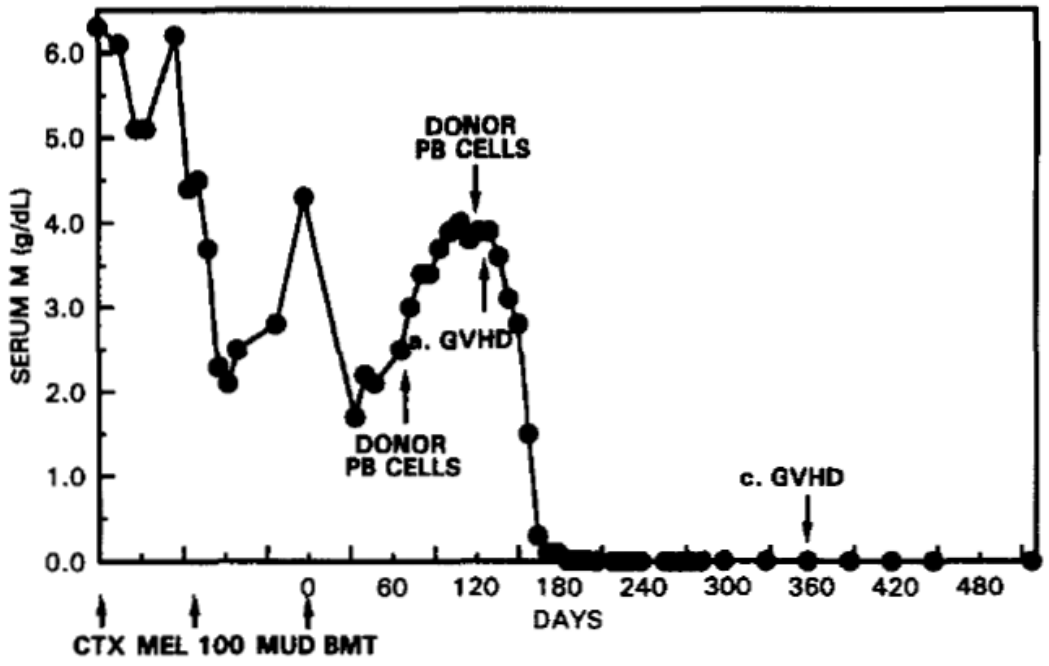
| | *N° of patients (%)* | | |
|---|---|---|---|
| | *MP (n=179)* | *VAD/MP (n=174)* | *VND/MP (n=174)* |
| Objective response | 95 (53) | 82 (47) | 86 (49) |
| Minor response | 25 (14) | 24 (14) | 21 (12) |
| No change | 28 (16) | 38 (22) | 34 (20) |
| Progression | 31 (17) | 30 (17) | 33 (19) |

# Graft-Versus-Myeloma Effect: Proof of Principle

By Guido Tricot, David H. Vesole, Sundar Jagannath, Jennifer Hilton, Nikhil Munshi, and Bart Barlogie

**The presence of a graft-versus-tumor effect has been well established in leukemia but not in multiple myeloma. A 40-year-old patient with myeloma refractory to standard chemotherapy and autologous transplantation received a matched unrelated T-cell–depleted transplant after conditioning with fractionated total-body irradiation, thiotepa, and cyclophosphamide. This procedure resulted in a transient and incomplete response with evidence of rapidly progressive disease within 2.5 months posttransplantation. The patient then received a small number of donor peripheral blood (PB) mononuclear cells (CD3 cells 1.2 × $10^6$/kg) without any further cytotoxic therapy. A complete remission was attained, lasting now for more than 14 months. The procedure was associated with severe acute and subsequently limited chronic graft-versus-host disease (GVHD). This report provides the first direct evidence of a graft-versus-myeloma effect after allogeneic transplantation.**

*© 1996 by The American Society of Hematology.*



# Prognostic Factors in Allogeneic Bone Marrow Transplantation for Multiple Myeloma

By Gösta Gahrton, Sante Tura, Per Ljungman, Joan Bladé, Lena Brandt, Michele Cavo, Thierry Façon, Alois Gratwohl, Anton Hagenbeek, Peter Jacobs, Antonio de Laurenzi, M. Van Lint, Mauricette Michallet, Jukka Nikoskelainen, Josy Reiffers, Diana Samson, Leo Verdonck, Theo de Witte, and Liisa Volin

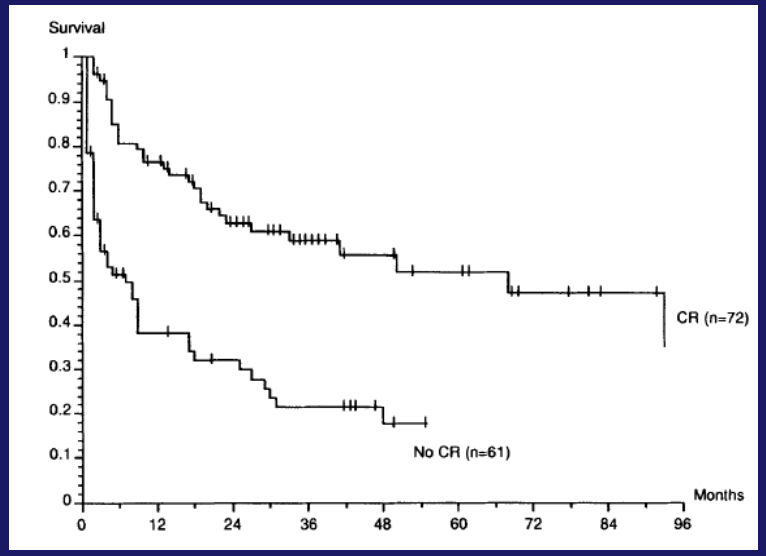
***Purpose:*** **To analyze prognostic factors for allogeneic bone marrow transplantation (BMT) in multiple myeloma.**

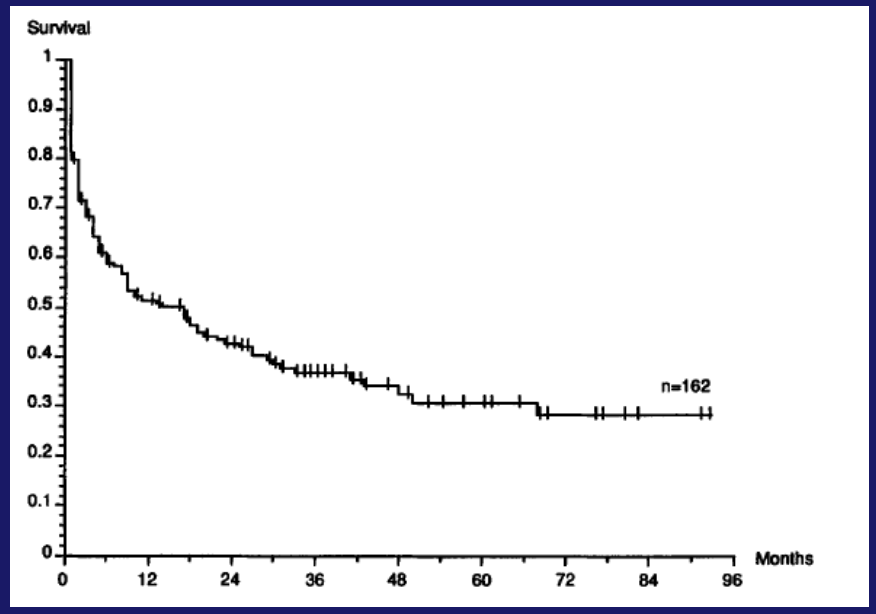
***Patients and Methods:*** **One hundred sixty-two reports of allogeneic matched sibling-donor transplants in multiple myeloma received by the European Group for Blood and Marrow Transplantation (EBMT) registry between 1983 and early 1993 were analyzed for prognostic factors. End points were complete remission, survival, and duration of complete remission.**

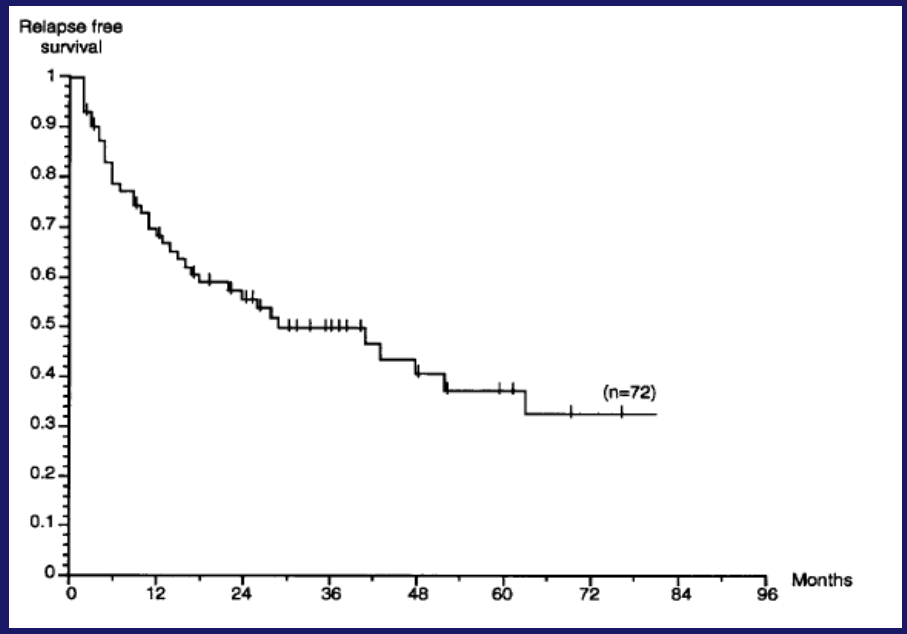
***Results:*** **Following BMT, 44% of all patients and 60% of assessable patients entered complete remission. The overall actuarial survival rate was 32% at 4 years and 28% at 7 years. The overall relapse-free survival rate of 72 patients who were in complete remission after BMT was 34% at 6 years. Favorable pretransplant prognostic factors for survival were female sex (41% at 4 years), stage I disease at diagnosis (52% at 4 years), one line of previous treatment (42% at 4 years), and being in complete remission before conditioning (64% at 3 years). The subtype immunoglobulin A (IgA) myeloma and a low $\beta_2$-microglobulin level (< 4 g/L) also tended to have a favorable prognostic impact. The most important post-transplant prognostic factor was to enter a complete remission. Grade III to IV graft-versus-host disease (GVHD) was associated with poor survival.**

***Conclusion:*** **Patients with a low tumor burden who respond to treatment before BMT and are transplanted after first-line therapy have the best prognosis following BMT.**

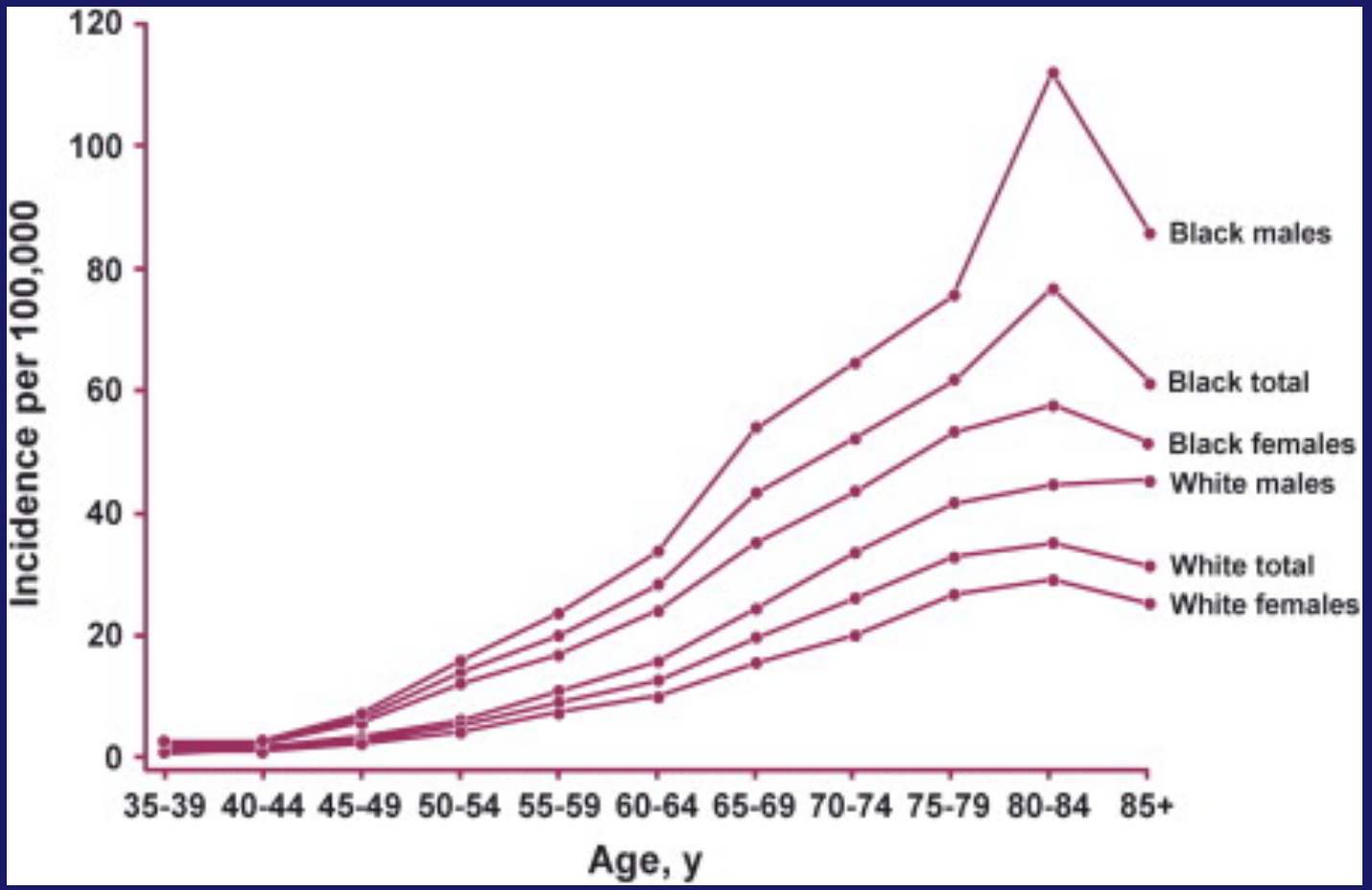
***J Clin Oncol 13:1312-1322. © 1995 by American Society of Clinical Oncology.***



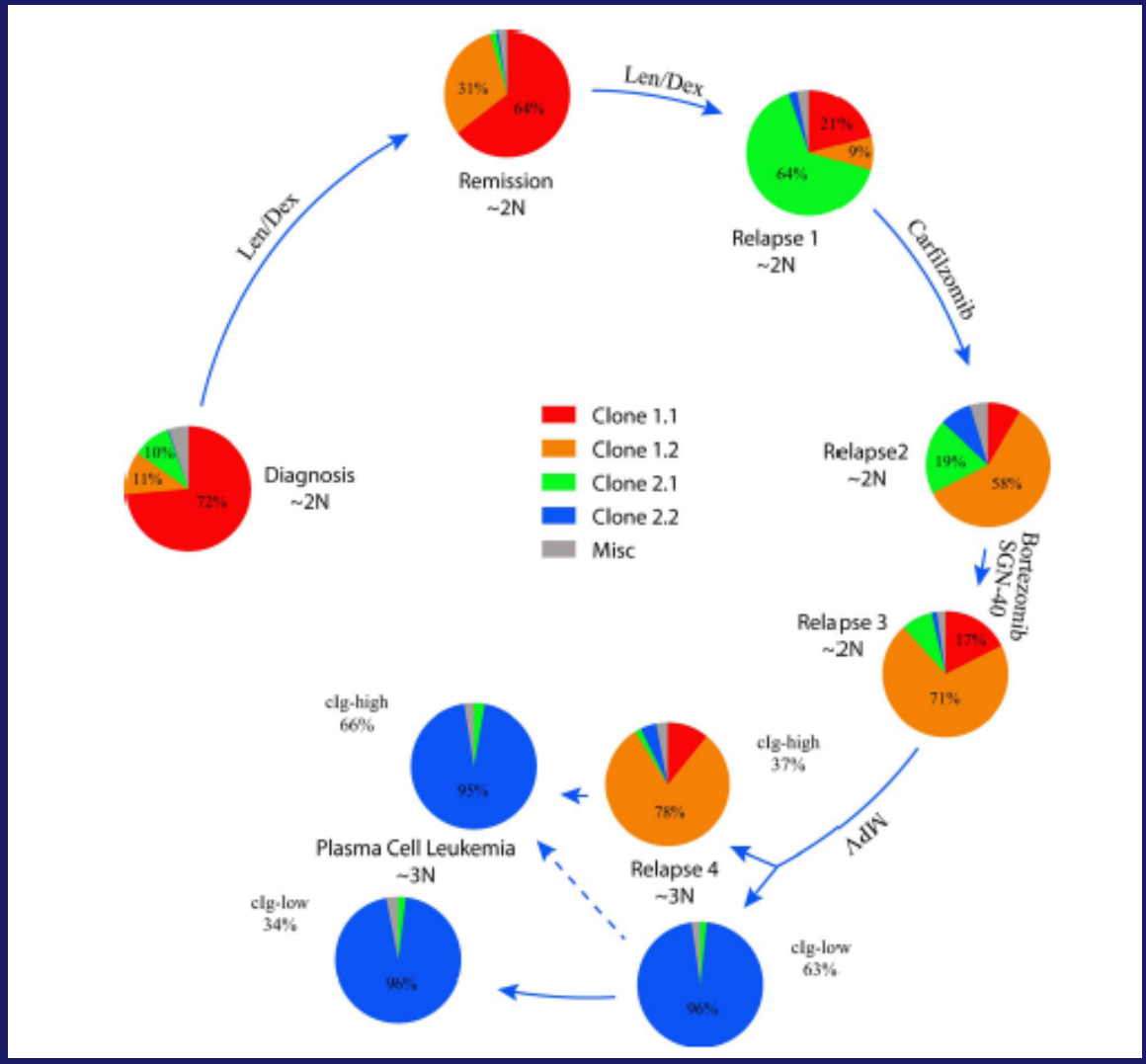



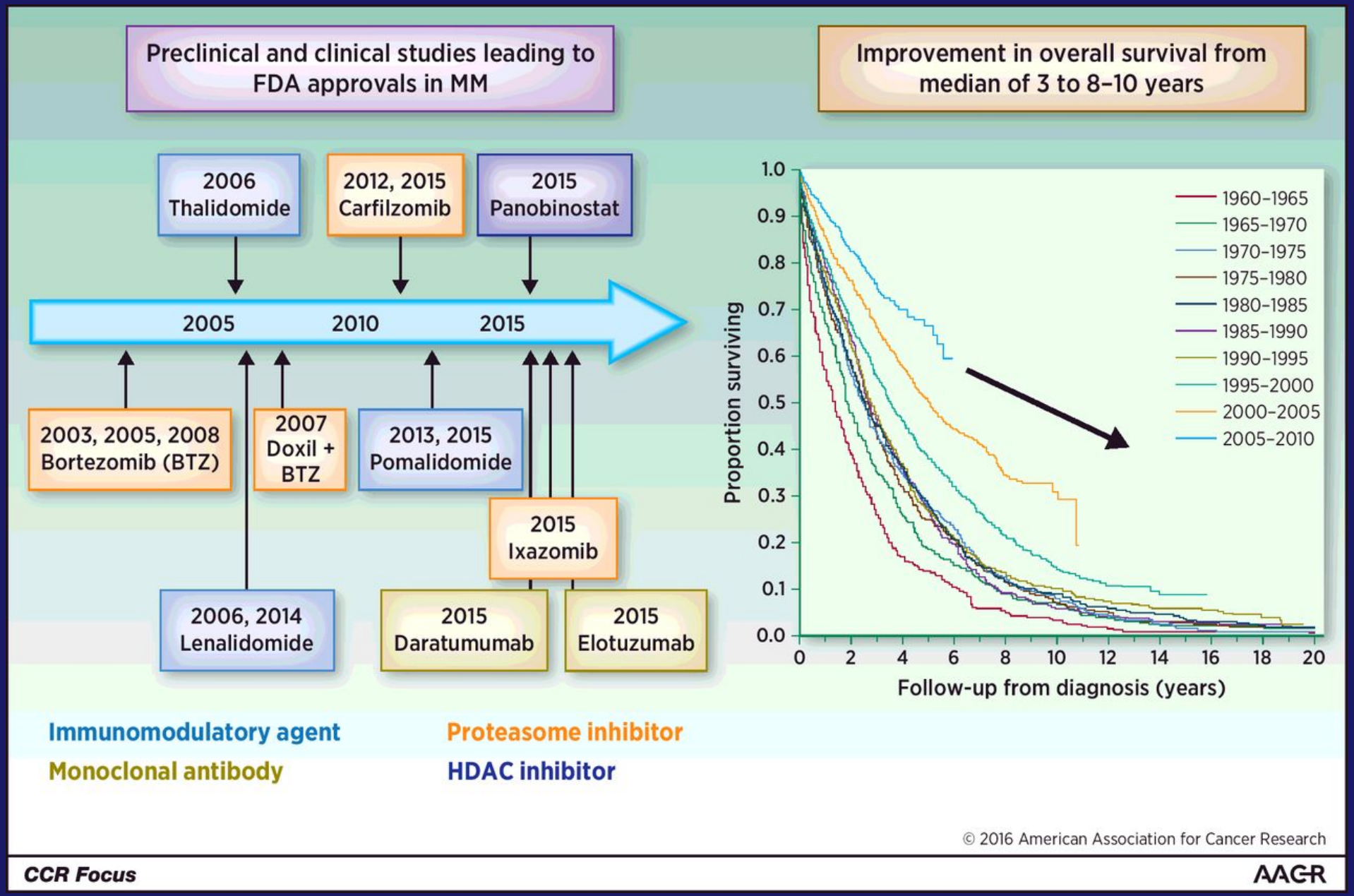
# Il mieloma è una malattia dell'anziano




Kyle et al, Best Pract Res Clin Haematol. 2007

**Il mieloma è una malattia in cui è evidente una evoluzione clonale**



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# Trapianti EBMT 2017

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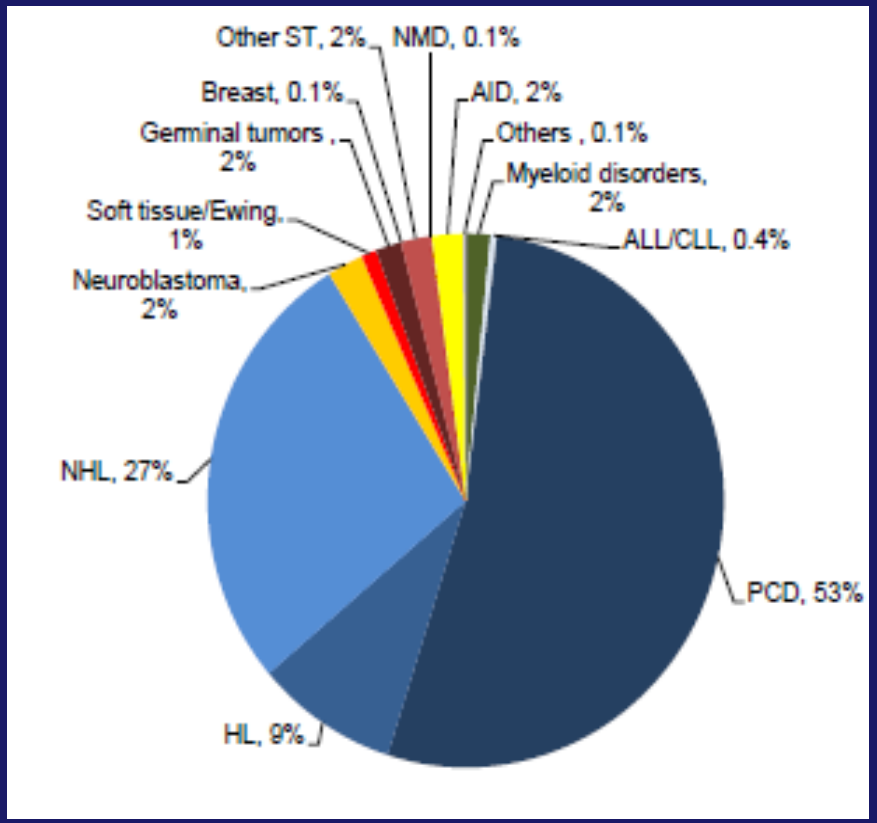
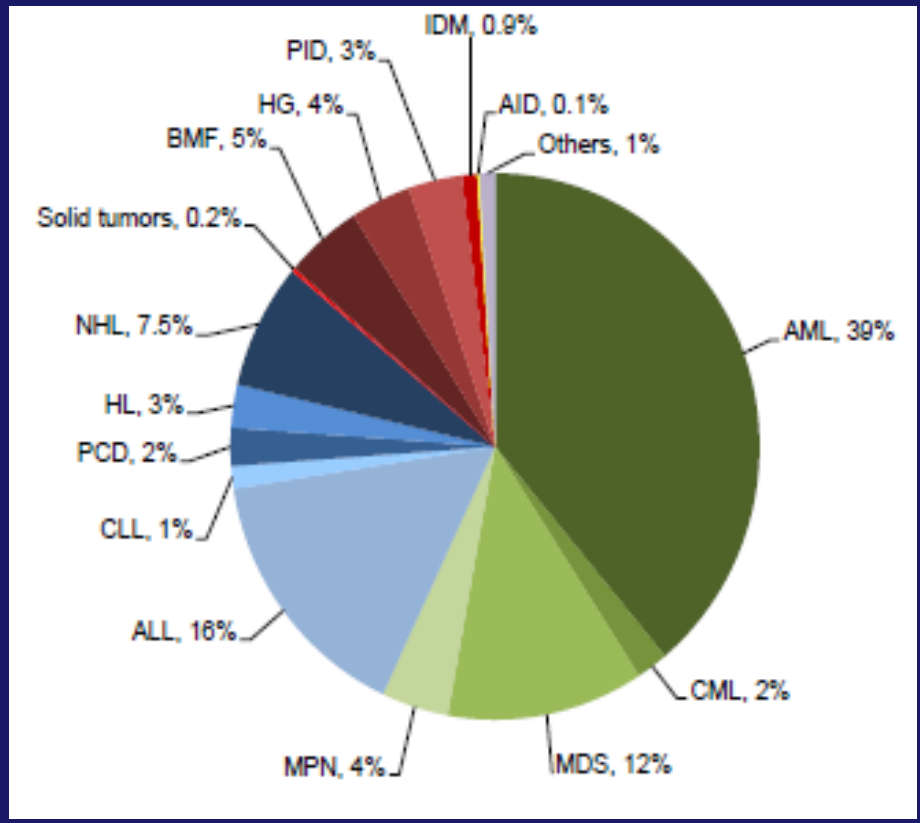



Allogenico



# Multiple myeloma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

P. Moreau[1], J. San Miguel[2], P. Sonneveld[3], M. V. Mateos[4], E. Zamagni[5], H. Avet-Loiseau[6], R. Hajek[7], M. A. Dimopoulos[8], H. Ludwig[9], H. Einsele[10], S. Zweegman[11], T. Facon[12], M. Cavo[5], E. Terpos[8], H. Goldschmidt[13], M. Attal[6] & C. Buske[14], on behalf of the ESMO Guidelines Committee*

Allogeneic SCT is not indicated as part of front-line therapy and should only be carried out in the context of a clinical trial.

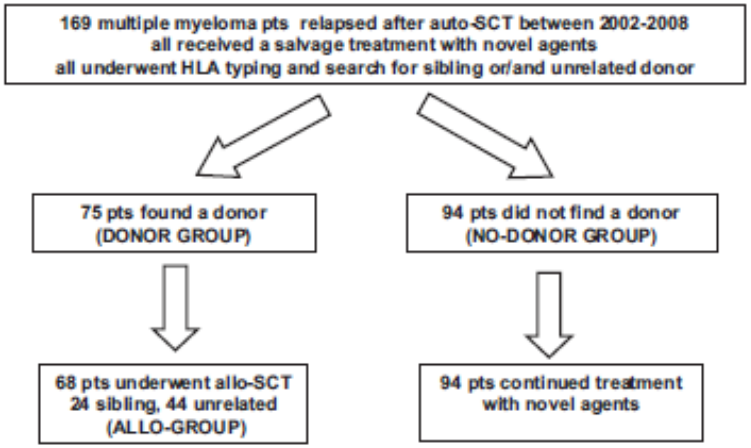
. In the relapse setting, allogeneic SCT should only be carried out in the context of a clinical trial.

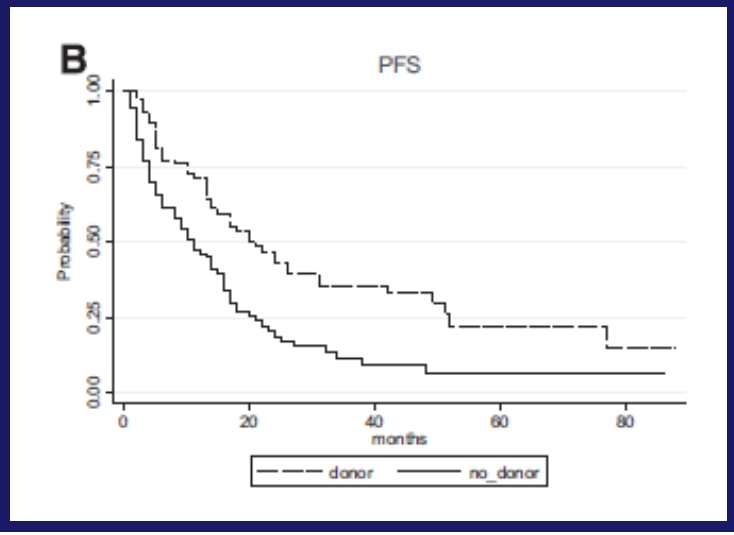
## Management of plasma cell leukaemia

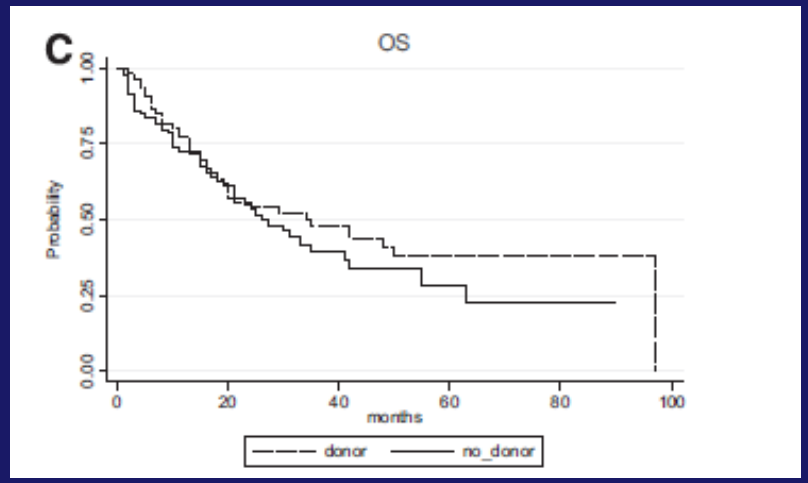
The role of novel agents such as monoclonal antibodies and immunotherapies, as well as metronomic approaches and allogeneic transplant should be formally investigated in these patients.

# Allogeneic Stem Cell Transplantation in Multiple Myeloma Relapsed after Autograft: A Multicenter Retrospective Study Based on Donor Availability

*Francesca Patriarca,[1] Hermann Einsele,[2] Francesco Spina,[3] Benedetto Bruno,[4] Miriam Isola,[5] Chiara Nozzoli,[6] Andrea Nozza,[7] Alessandra Sperotto,[1] Fortunato Morabito,[8] Gernot Stuhler,[2] Moreno Festuccia,[4] Alberto Bosi,[6] Renato Fanin,[1] Paolo Corradini[9]*

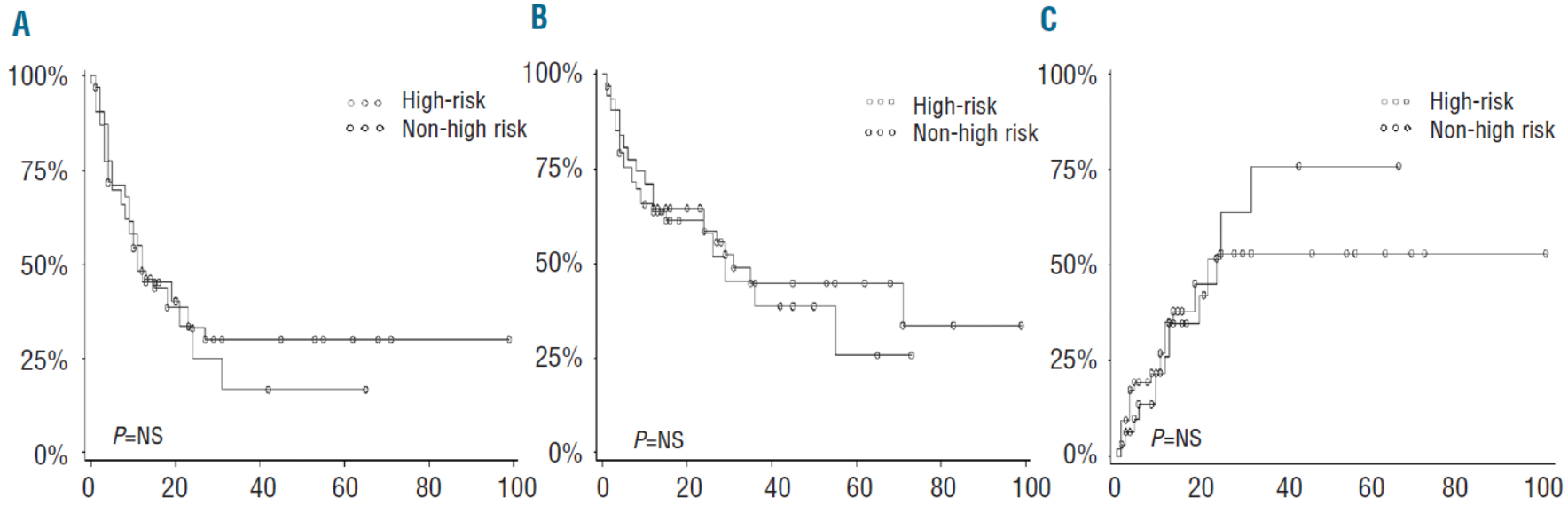


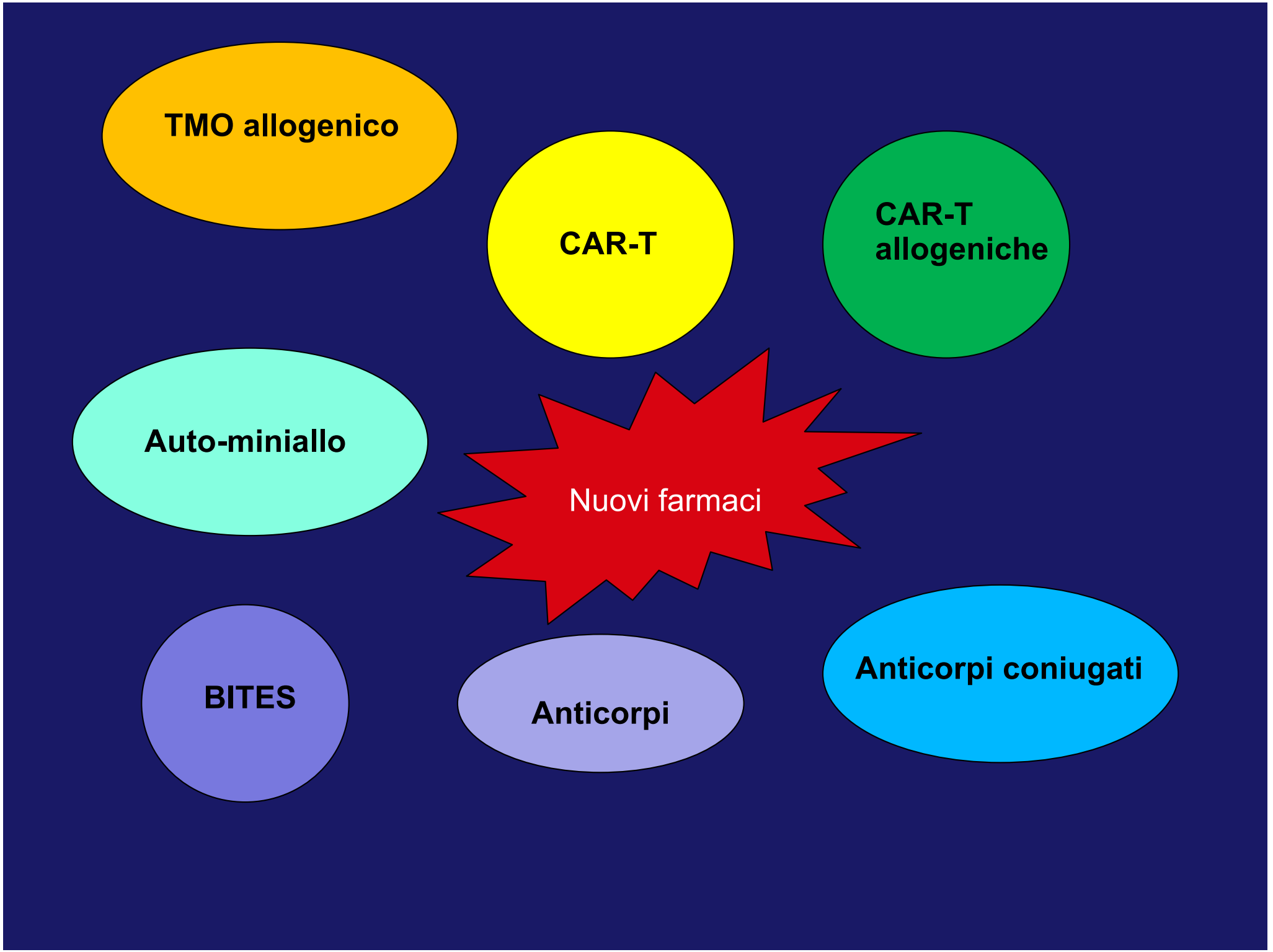



# Impact of genetic abnormalities after allogeneic stem cell transplantation in multiple myeloma: a report of the Société Française de Greffe de Moelle et de Thérapie Cellulaire

Damien Roos-Weil,[1] Philippe Moreau,[2] Hervé Avet-Loiseau,[3] Jean-Louis Golmard,[4] Mathieu Kuentz,[5] Stéphane Vigouroux,[6] Gérard Socié,[7] Sabine Furst,[8] Jean Soulier,[9] Steven Le Gouill,[2] Sylvie François,[10] Anne Thiebaut,[11] Agnès Buzyn,[12] Natacha Maillard,[13] Ibrahim Yakoub-Agha,[14] Nicole Raus,[15] Jean-Paul Fermand,[16] Mauricette Michallet,[17] Didier Blaise,[8] and Nathalie Dhédin[1] for the Société Française de Greffe de Moelle et de Thérapie Cellulaire (SFGM-TC)




TMO allogenico
CAR-T
CAR-T allogeniche
Auto-miniallo
Nuovi farmaci
BITES
Anticorpi
Anticorpi coniugati