Conditioning regimens in MPD patients

Strong graft-versus-MF effect has been suggested by several reports showing excellent responses to donor lymphocyte infusions and to immunosuppression reduction for treating posttransplant relapse.

Despite the strong graft-versus-tumor effect, the choice and the intensity of conditioning regimen seem to have important role with notable increased graft failure and/or relapse rates when using nonmyeloablative or reduced intensity regimens.

Conditioning regimens:

- There is consensus that nonmyeloablative regimens should be avoided in MF patients.

- There are no randomized studies comparing reduced intensity to MAC, but myeloablative regimens are generally preferred for young and fit patients.

- Furthermore, transplant-related toxicities were high with conditioning regimens incorporated high-dose cyclophosphamide, total body irradiation (TBI), and/or fixed dose busulfan (Bu)-based regimens.

Conditioning regimens:

- prospective phase 2 studies conducted by the EBMT and included 103 patients with MF (median age of 55 years) who all received reducedintensity conditioning (RIC) with Bu and fludarabine (Flu), the 5-year OS rate was 67% with NRM of 16% at 1 year, and cumulative incidence of relapse of 22% at 3 years.

- Age was found to be a strong predictor for survival in this study, with a 5-year OS of 48% for patients at age > 55 years compared to 82% in the younger age group.

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CLINICAL TRIALS AND OBSERVATIONS | DECEMBER 17, 2009

Allogeneic stem cell transplantation after reduced-intensity conditioning in patients with myelofibrosis: a prospective, multicenter study of the Chronic Leukemia Working Party of the European Group for Blood and Marrow Transplantation

Clinical Trials & Observations

Nicolaus Kröger, Ernst Holler, Guido Kobbe, Martin Bornhäuser, Rainer Schwerdtfeger, Herrad Baurmann, Arnon Nagler, Wolfgang Bethge, Matthias Stelljes, Lutz Uharek, Hannes Wandt, Andreas Burchert, Paolo Corradini, Jörg Schubert, Martin Kaufmann, Peter Dreger, Gerald G. Wulf, Hermann Einsele, Tatjana Zabelina, Hans Michael Kvasnicka, Jürgen Thiele, Ronald Brand, Axel R. Zander, Dietger Niederwieser, Theo M. de Witte

In the largest EBMT registry study, which included 2224 patients with MF (35% received MAC), there was a trend for increased relapse with RIC but no OS differences.

However, with regards to the composite endpoint of GVHD-free/relapse-free survival (GRFS), the 5-year GRFS was inferior in the reduced intensity group (26.1% vs. 32.4% for MAC; $P = .001$).

Age, donor type, and performance status were predictive for outcomes in both groups. The authors concluded that MAC should remain a preferred choice for younger and fit MF patients.

Biology of Blood and Marrow Transplantation

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Myeloablative and Reduced-Intensity Conditioned Allogeneic Hematopoietic Stem Cell Transplantation in Myelofibrosis: A Retrospective Study by the Chronic Malignancies Working Party of the European Society for Blood and Marrow Transplantation

Donal McLornan[1,*], Richard Szydlo[2], Linda Koster[3], Yves Chalandon[4], Marie Robin[5], Christine Wolschke[6], Dietrich Beelen[7], Gerard Socié[5], Martin Bornhäuser[8], Emanuele Angelucci[9], Dietger Niederwieser[10], Arnim Gerbitz[11], Jürgen Finke[12], Antonin Vitek[13], Maija Itälä-Remes[14], Aleksandar Radujkovic[15], Lothar Kanz[16], Victoria Potter[17], Patrice Chevallier[18], Matthias Stelljes[19], Eefke Petersen[20], Stephen Robinson[21], Xavier Poiré[22], Evgeny Klyuchnikov[6], Juan Carlos Hernández-Boluda[23], Tomasz Czerw[24], Patrick Hayden[25], Nicolaus Kröger[6], Ibrahim Yakoub-Agha[26]

[1] *Department of Haematology, Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom*

long-term outcomes from a phase 2 study showing improved MF outcomes using a pharmacokinetic-monitored MAC conditioning (BuFlu) compared to RIC.

At a median follow-up of 5.1 years, the 3-year OS, relapse, and NRM rates were 74%, 32.3%, and 9.7%, respectively, in the MAC group compared to 60%,

53.3%, and 20%, respectively, in the RIC group.

The DIPSS-plus score was found to be the only independent prognostic factor for event-free survival, and both high-risk DIPSS-plus and older age were predictors for inferior OS.

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Optimizing the Conditioning Regimen for Hematopoietic Cell Transplant in Myelofibrosis: Long-Term Results of a Prospective Phase II Clinical Trial

Uday Popat[1,*], Rohtesh S. Mehta[1], Roland Bassett[2], Piyanuch Kongtim[1,3], Julianne Chen[1], Amin M. Alousi[1], Paolo Anderlini[1], Stefan Ciurea[1], Chitra Hosing[1], Roy Jones[1], Partow Kebriaei[1], Issa Khouri[1], Richard Lindsay PA[1], Yago Nieto[1], Amanda Olson[1], Betul Oran[1], Muzaffar H. Qazilbash[1], Gabriela Rondon[1], Elizabeth J. Shpall[1], Srdan Verstovsek[1], Borje S. Andersson[1], Richard E. Champlin[1]

[1] *Department of Stem Cell Transplantation and Cellular Therapy, University of Texas M.D. Anderson Cancer Center, Houston, Texas*
[2] *Department of Biostatistics, University of Texas M.D. Anderson Cancer Center, Houston, Texas*