

Thomas Jefferson University Jefferson Digital Commons

Department of Medical Oncology Faculty Papers

Department of Medical Oncology

2-16-2013

A 2-Step Approach to Myeloablative Haploidentical Stem Cell Transplantation with Optimized T-Cell Dosing: Early Immune Reconstitution Leads to Better Outcomes

Sameh Gaballa

Thomas Jefferson University Hospital, samehgaballa@gmail.com

Onder Alpdogan

Thomas Jefferson University Hospital, Seyfettin.Alpdogan@jefferson.edu

Matthew Carabasi

Thomas Jefferson University, Matthew.Carabasi@jefferson.edu

Joanne Filicko

Thomas Jefferson University, Joanne. Filicko-O'Hara@jefferson.edu

Margaret Kasner

Thomas Jefferson University, Margaret.Kasner@jefferson.edu

Lettus know how access to this document benefits you

Follow this and additional works at: http://jdc.jefferson.edu/medoncfp



Part of the <u>Hematology Commons</u>, and the <u>Oncology Commons</u>

Recommended Citation

Gaballa, Sameh; Alpdogan, Onder; Carabasi, Matthew; Filicko, Joanne; Kasner, Margaret; Martinez-Outshoorn, MD, Ubaldo E.; Wagner, John L; Weiss, Mark; Flomenberg, Neal; and Grosso, Delores, A 2-Step Approach to Myeloablative Haploidentical Stem Cell Transplantation with Optimized T-Cell Dosing: Early Immune Reconstitution Leads to Better Outcomes" (2013). Department of Medical Oncology Faculty Papers. Paper 16.

http://jdc.jefferson.edu/medoncfp/16

This Article is brought to you for free and open access by the Jefferson Digital Commons. The Jefferson Digital Commons is a service of Thomas Jefferson University's Center for Teaching and Learning (CTL). The Commons is a showcase for Jefferson books and journals, peer-reviewed scholarly publications, unique historical collections from the University archives, and teaching tools. The Jefferson Digital Commons allows researchers and interested readers anywhere in the world to learn about and keep up to date with Jefferson scholarship. This article has been accepted for inclusion in

Authors Sameh Gaballa; Onder Alpdogan; Matthew Carabasi; Joanne Filicko; Margaret Kasner; Ubaldo E. Martinez- Outshoorn, MD; John L Wagner; Mark Weiss; Neal Flomenberg; and Delores Grosso

A 2-Step Approach to Myeloablative Haploidentical Stem Cell Transplantation with Optimized T-Cell Dosing: Early Immune Reconstitution Leads to Better Outcomes

Track: BMT Tandem "Scientific" Meeting

Saturday, February 16, 2013, 4:45 PM-6:45 PM

Ballroom A-D (Salt Palace Convention Center)

<u>Sameh Gaballa, MD</u>, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Onder Alpdogan, MD, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Matthew Carabasi, MD, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Joanne Filicko, MD , Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Margaret Kasner, MD , Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Ubaldo Martinez, MD, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

John L. Wagner, MD, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Mark Weiss, MD , Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Neal Flomenberg, MD, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

Dolores Grosso, DNP, Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

We developed a 2-step approach to myeloablative haploidentical HSCT in which patients receive a large fixed dose of cyclophosphamide (CY)-tolerized T cells separately frm the HSC infusion in the hopes of accelerating post HSCT immune reconstitution (IR). The uniformity of the T cell dosing facilitates comparison of patients without (low risk) and with (high risk) active malignancy at HSCT to ascertain the impact of disease status at HSCT on IR with fewer confounding effects from conditioning or T cell dosing.

We analyzed IR at day +28 in patients receiving 2 step myeloablative haploidentical HSCT. All patients received 12 Gy of total body irradiation followed by 2 x 10^8 CD3+ cells/kg donor T cells (HSCT step 1). CY 60 mg/kg/d x 2 was given starting 2 or 3 days after the T cell infusion in the low and high risk groups respectively. Tacrolimus and MMF were begun on day -1. A CD 34 selected product was infused on day 0 (HSCT step 2) with median CD34 doses of 5.8 and 5.2 x 10^6 /kg in the low and high-risk groups respectively.

19 patients with AML (9), ALL (7), MDS (1), and NHL (2) without disease, and 16 patients with AML (10), ALL (2), MDS (3), and T cell NHL (1) with active disease at HSCT were analyzed. A 17th patient in the high risk group died prior to engraftment and was not fully evaluable. Outcomes for the low and high risk groups respectively with 2-24 months follow-up (median of

9 in each group) were: no rejections; ANC >500: 11 versus 12 days; grades III-IV GVHD: 5.2% versus 18.7%; mortality from GVHD 0% versus 6.2%; infectious mortality: 0% versus 12.5%; non-infectious regimen-related mortality: 0% versus 11.7%; mortality from relapse; 5.2% versus 18.7%; Overall survival: 94.8% versus 52.9%. By day +28, all patients had achieved CR and >95% donor marrow chimerism. Compared to our experience with T cell depleted (TCD) HSCT, improved T and NK cell IR was observed, although the low risk group had higher median numbers of T cells. Conversely, higher numbers of CD56^{bright} NK cells were present in the high risk group.

Compared to TCD approaches at our institution and others, the 2 step approach allows for stronger early IR with low infectious mortality in patients without and with active malignancy at HSCT. IR was more robust in patients without active disease. IR in the higher risk group may be hindered by less hospitable marrow stroma and a greater baseline inflammation related to the active malignancy and exacerbated by the HSCT. The increased rate of significant GVHD and the prominence of NK cells, which are strong producers of cytokines, may reflect this higher state of inflammation. In addition, differences in the degree of T cell eradication by CY, based on T cell responses to malignancy or the longer period of T cell activation in the high risk regimen, may account for variations in IR between the groups. Recognition of the differences in early IR amongst specific patient populations may help optimize post HSCT care.

