

Progress in chronic graft-versus-host disease

Paul J. Martin

Fred Hutchinson Cancer
Research Center, University of
Washington, Seattle, WA, USA

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Corresponding author:

Paul J. Martin
Fred Hutchinson Cancer Research Center
University of Washington,
Seattle, WA, USA
pmartin@fnrc.org

www.rbhh.org or www.scielo.br/rbhh

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The National Institute of Health (NIH) consensus conference on criteria for clinical trials in chronic graft-versus-host disease (GvHD) brought fresh attention to a problem that is all too familiar to clinicians involved in hematopoietic stem cell transplantation. The series of 6 papers published in 2005 proposed new diagnostic criteria for the disease, summarized information regarding biomarkers and pathologic features associated with the disease, and offered recommendations for supportive care, measurement of response to treatment and the conduct of clinical trials.⁽¹⁻⁶⁾

Subsequent publications have focused on efforts to validate the diagnostic criteria through retrospective studies and some additional work has been done to elucidate the significance of biomarkers, especially those indicating a possible role for B cells in the pathogenesis of the disease. In the United States, Dr. Stephanie Lee organized a consortium of investigators in multiple centers to collect prospective data from a large cohort of incident and prevalent cases. These data are now being used to address several important questions, including the optimal methods for measuring ocular and oral involvement, the association of disease severity with quality of life and risk of mortality, and the prognostic significance of acute GvHD manifestations including cutaneous erythema and gastrointestinal and hepatic involvement. Ultimately, the results of these studies will be used to refine and validate recommendations that emerged from the NIH consensus conference, which were mostly based on expert opinion.

In this issue of the *Revista Brasileira de Hematologia e Hemoterapia*, Vigorito and colleagues describe the initial results of work by a group of Brazilian investigators to develop a platform for collaboration in clinical trials related to chronic GvHD.⁽⁷⁾ These investigators translated the US prospective data forms into Portuguese and then tested their use in five Brazilian centers. To date, the study has enrolled 34 patients with chronic GvHD. The Brazilian group and their colleagues in the US are to be congratulated for this first demonstration that international collaborations in the field of chronic GvHD are feasible in an academic setting.

Much work lies ahead. The authors emphasize the theme that the Brazilian consortium is intended to serve as a platform for future collaboration in clinical trials. Better insight into the pathogenesis of chronic GvHD is needed in order to select treatments that are most likely to be effective and safe. Further discussion is needed in order to standardize eligibility criteria, organ and overall response criteria, and assessment time points in studies of secondary treatment for chronic GvHD. The "shared language" emerging from this standardization will facilitate informative comparisons of results between different studies. Even more importantly, benchmarks of success should be established from both retrospective and prospective cohorts so that adequately powered, rigorous phase II studies can be conducted with one-sample statistical methods to identify the most promising agents for testing in future phase III trials.

The case-report forms used by the US and Brazilian consortiums will benefit from further refinement, since their current length and complexity is likely to discourage physicians from enrolling patients in clinical trials. The analysis of data from the forms will help to identify the most reliable and useful items that should be retained in shorter and less complex report forms to be used for future clinical trials. Members of the Brazilian consortium are in a good position to suggest how the forms can be improved since they were not involved in the design. As a more important contribution, however, the current members should celebrate the success illustrated in this report as a way of recruiting additional Brazilian colleagues to join in this new international effort to improve the treatment of patients with chronic GvHD.

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