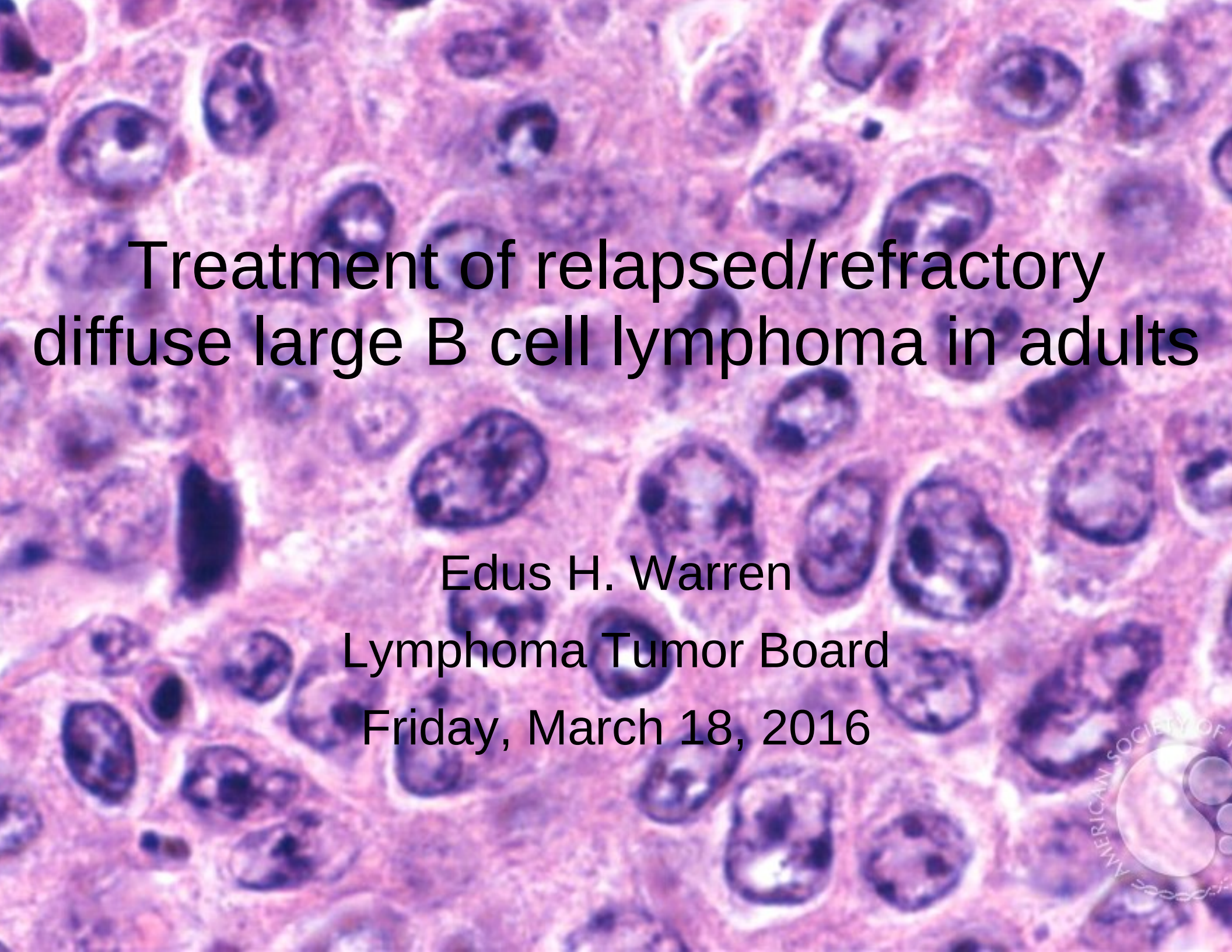


Treatment of relapsed/refractory diffuse large B cell lymphoma in adults

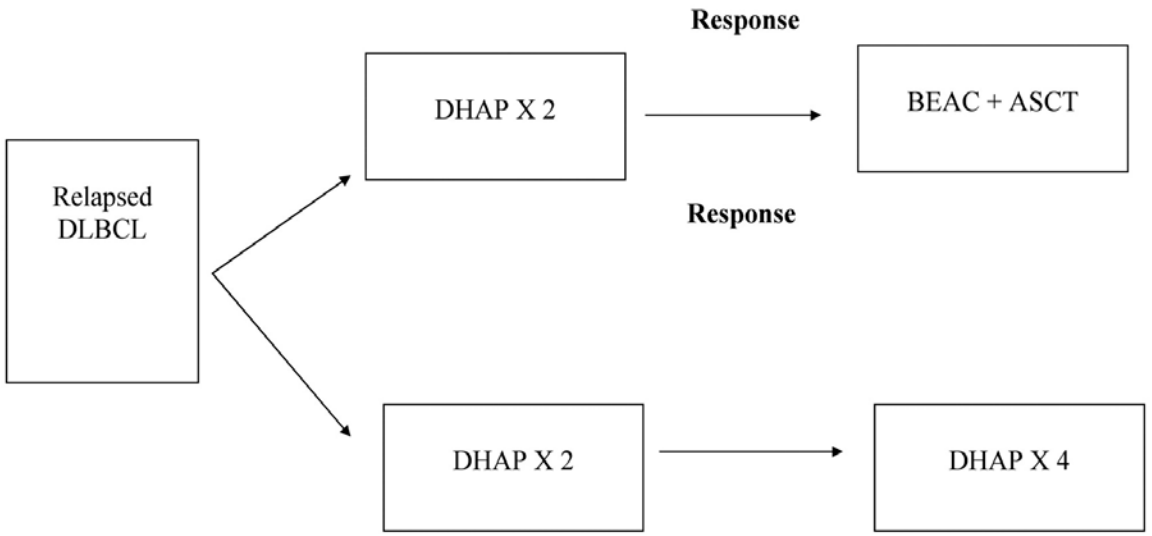
Edus H. Warren

Lymphoma Tumor Board

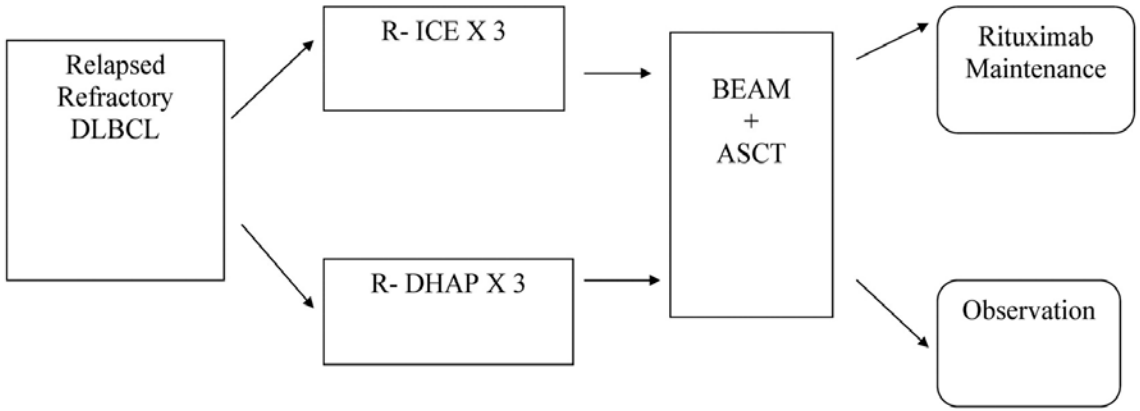
Friday, March 18, 2016

PARMA and CORAL study schemas

A: PARMA Study



B: CORAL STUDY



Jonathan W. Friedberg Hematology 2011;2011:498-505

AUTOLOGOUS BONE MARROW TRANSPLANTATION AS COMPARED WITH SALVAGE CHEMOTHERAPY IN RELAPSES OF CHEMOTHERAPY-SENSITIVE NON-HODGKIN'S LYMPHOMA

THIERRY PHILIP, M.D., CESARE GUGLIELMI, M.D., ANTON HAGENBEEK, M.D., RENIER SOMERS, M.D., HANS VAN DER LELIE, M.D., DOMINIQUE BRON, M.D., PIETER SONNEVELD, M.D., CHRISTIAN GISSELBRECHT, M.D., JEAN-YVES CAHN, M.D., JEAN-LUC HAROUSSEAU, M.D., BERTRAND COIFFIER, M.D., PIERRE BIRON, M.D., FRANCO MANDELLI, M.D., AND FRANCK CHAUVIN, M.D.

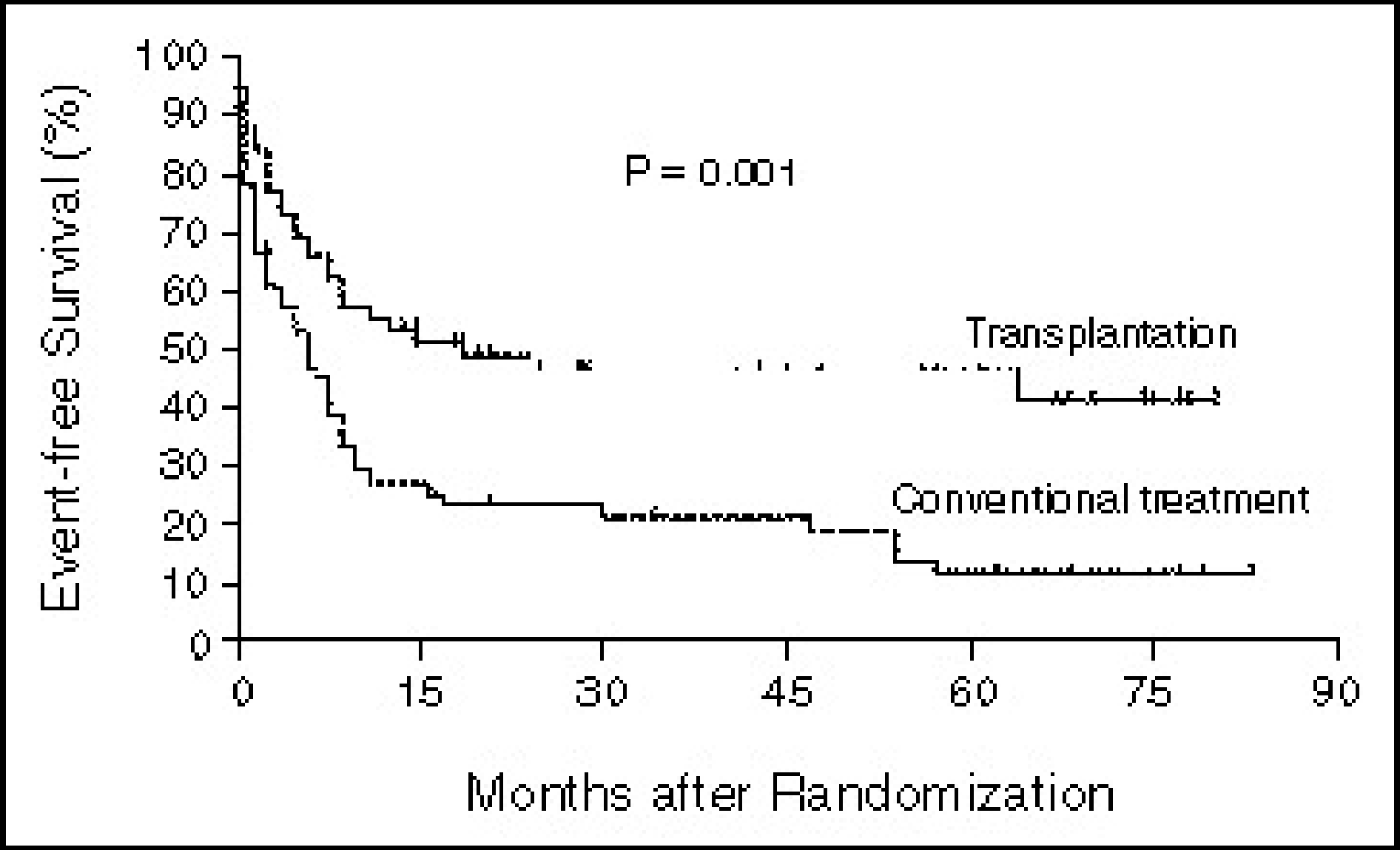
Abstract *Background.* High-dose chemotherapy followed by autologous bone marrow transplantation is a therapeutic option for patients with chemotherapy-sensitive non-Hodgkin's lymphoma who have relapses. In this report we describe a prospective randomized study of such treatment.

Methods. A total of 215 patients with relapses of non-Hodgkin's lymphoma were treated between July 1987 and June 1994. All patients received two courses of conventional chemotherapy. The 109 patients who had a response to chemotherapy were randomly assigned to receive four courses of chemotherapy plus radiotherapy (54 patients) or radiotherapy plus intensive chemotherapy and autologous bone marrow transplantation (55 patients).

Results. The overall rate of response to conventional chemotherapy was 58 percent; among patients with relapses after chemotherapy, the response rate was 64 percent, and among those with relapses during chemotherapy, the response rate was 21 percent. There were three deaths from toxic effects among the patients in the transplantation group, and none among those in the group receiving chemotherapy without transplantation. The two groups did not differ in terms of prognostic factors. The median follow-up time was 63 months. The response rate was 84 percent after bone marrow transplantation and 44 percent after chemotherapy without transplantation. At five years, the rate of event-free survival was 46 percent in the transplantation group and 12 percent in the group receiving chemotherapy without transplantation ($P = 0.001$), and the rate of overall survival was 53 and 32 percent, respectively ($P = 0.038$).

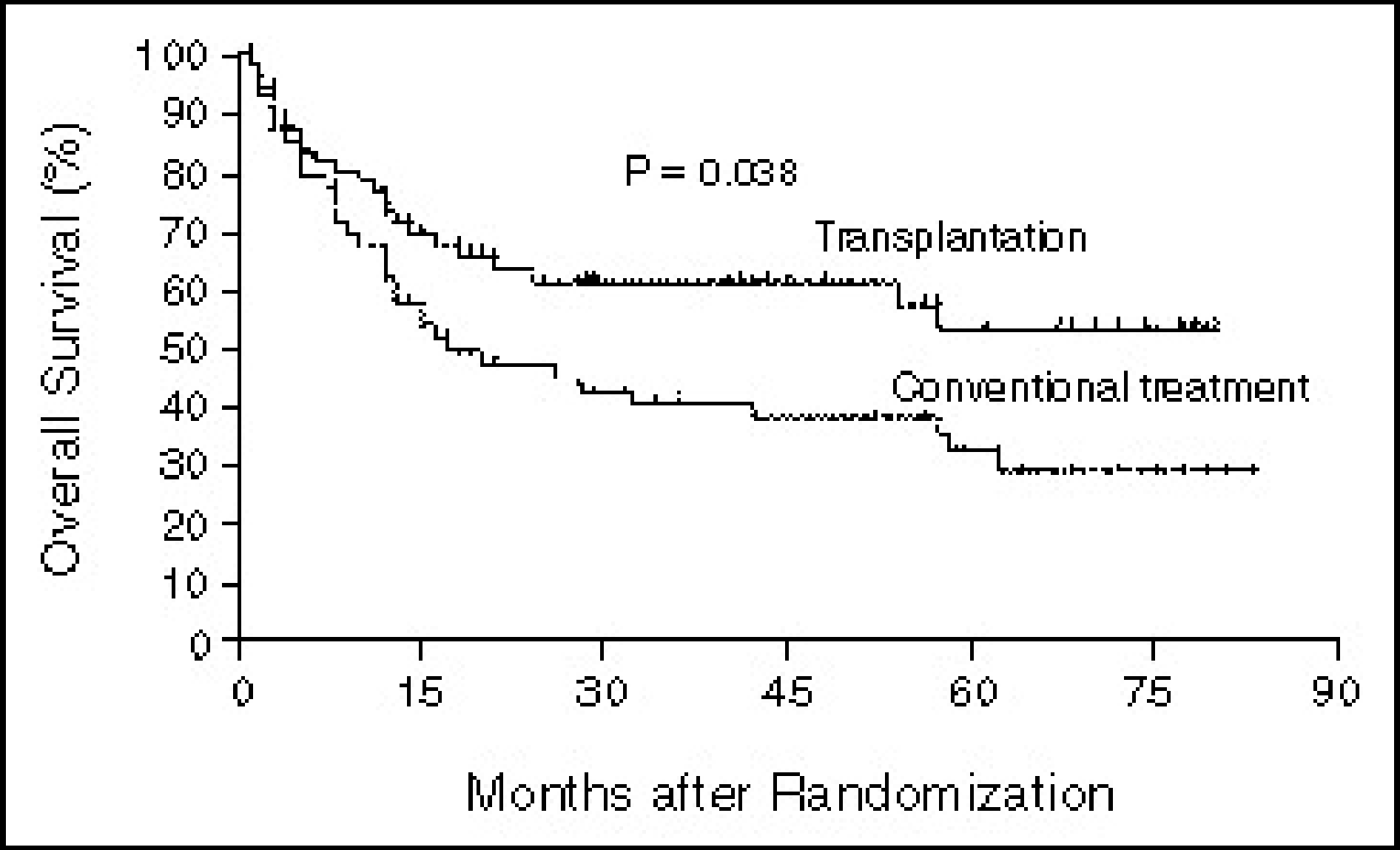
Conclusions. As compared with conventional chemotherapy, treatment with high-dose chemotherapy and autologous bone marrow transplantation increases event-free and overall survival in patients with chemotherapy-sensitive non-Hodgkin's lymphoma in relapse. (N Engl J Med 1995;333:1540-5.)

Kaplan–Meier Curves for Event-free Survival of Patients in the Transplantation and Conventional-Treatment Groups.



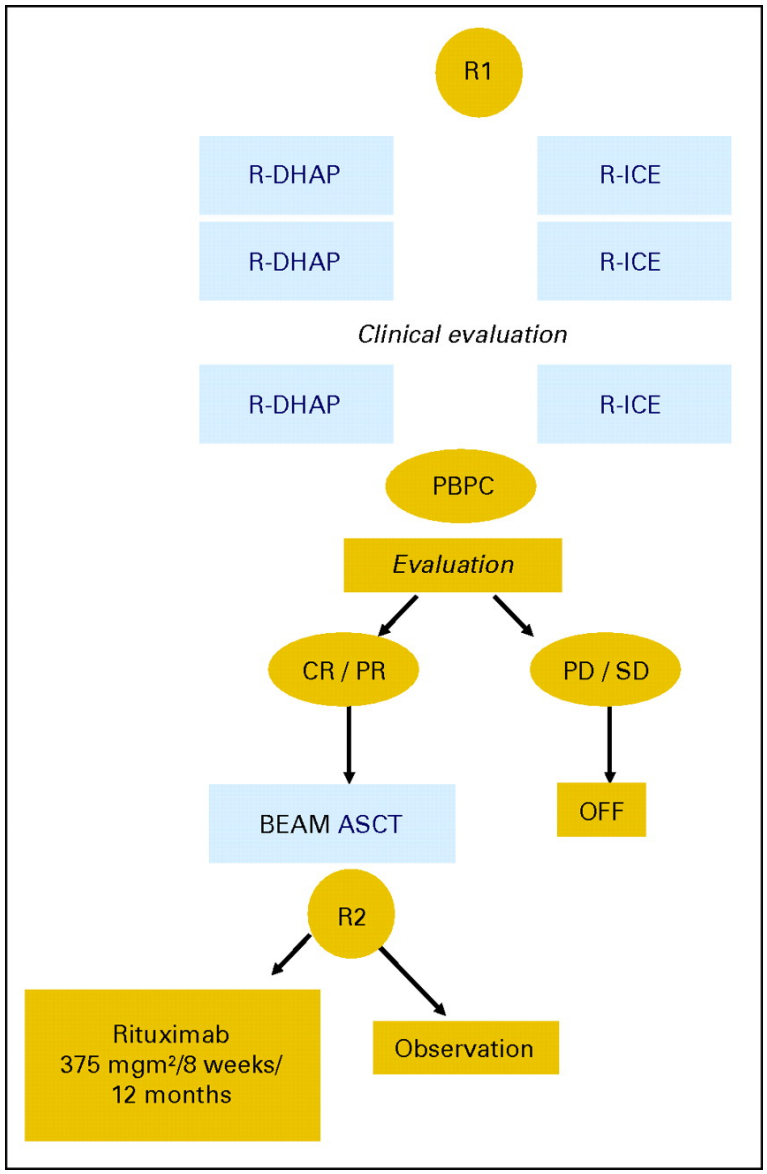
Philip T et al. N Engl J Med 1995;333:1540-1545.

Kaplan–Meier Curves for Overall Survival of Patients in the Transplantation and Conventional-Treatment Groups.



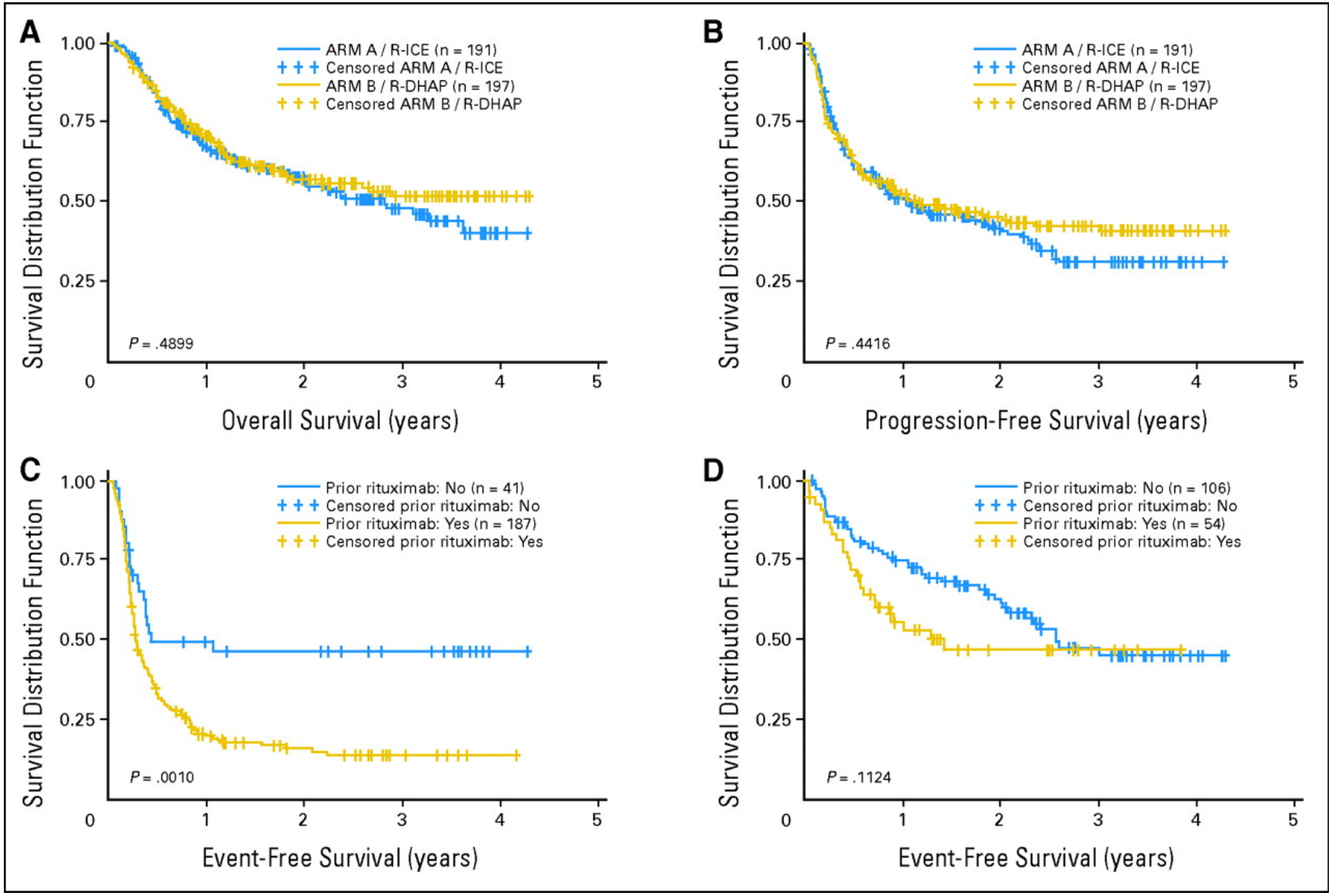
Philip T et al. N Engl J Med 1995;333:1540-1545.

CORAL Treatment protocol



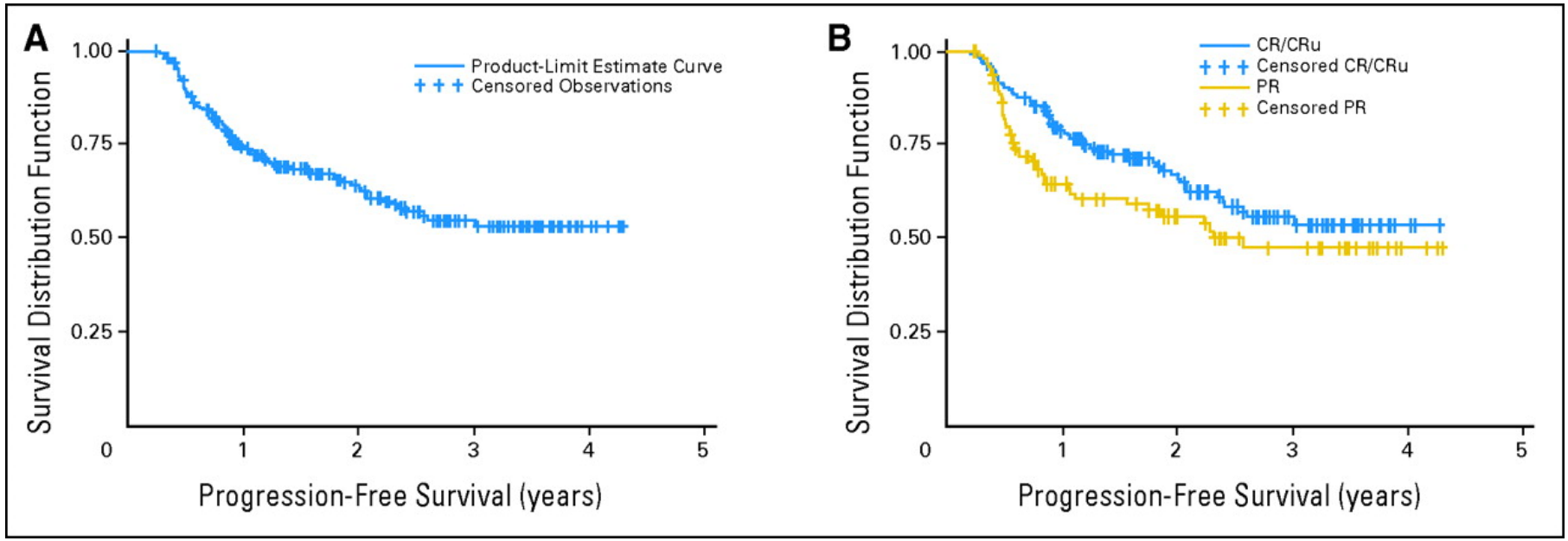
Christian Gisselbrecht et al. JCO 2010;28:4184-4190

Survival according to the first random assignment (intent to treat) - CORAL



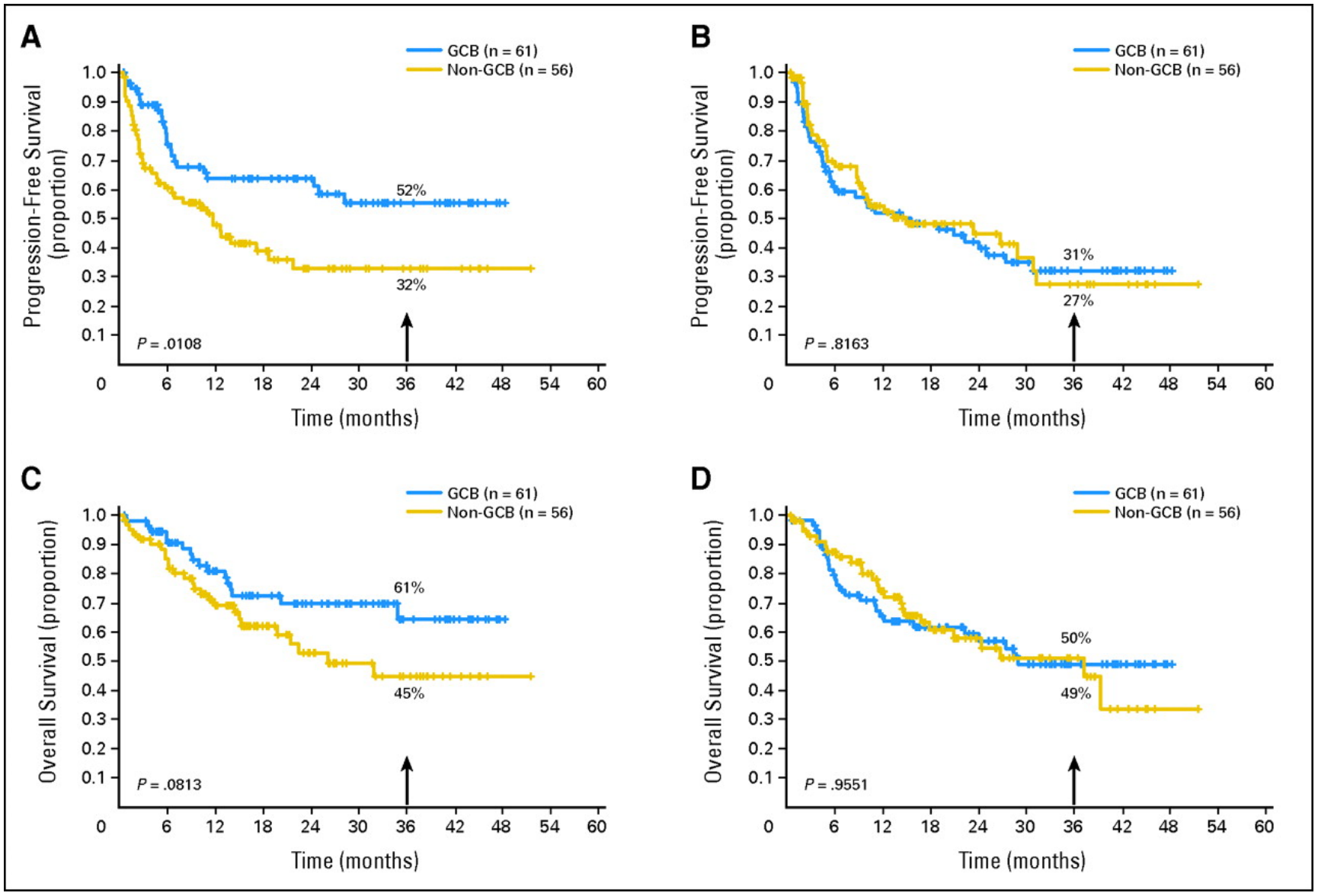
Christian Gisselbrecht et al. JCO 2010;28:4184-4190

Progression-free survival (PFS) of patients undergoing autologous stem-cell transplantation (intent to treat; n = 206) – CORAL



Christian Gisselbrecht et al. JCO 2010;28:4184-4190

Progression-free survival and overall survival according to the (A, C) rituximab, dexamethasone, high-dose cytarabine, and cisplatin (R-DHAP) versus (B, D) rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) treatment arms - CORAL



Catherine Thieblemont et al. JCO 2011;29:4079-4087

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ORIGINAL REPORT

Randomized Comparison of Gemcitabine, Dexamethasone, and Cisplatin Versus Dexamethasone, Cytarabine, and Cisplatin Chemotherapy Before Autologous Stem-Cell Transplantation for Relapsed and Refractory Aggressive Lymphomas: NCIC-CTG LY.12

Michael Crump, John Kuruvilla, Stephen Couban, David A. MacDonald, Vishal Kukreti, C. Tom Kouroukis, Morel Rubinger,† Rena Buckstein, Kevin R. Imrie, Massimo Federico, Nicola Di Renzo, Kang Howson-Jan, Tara Baetz, Leonard Kaizer, Michael Voralia, Harold J. Olney, A. Robert Turner, Jonathan Sussman, Annette E. Hay, Marina S. Djurfeldt, Ralph M. Meyer, Bingshu E. Chen, and Lois E. Shepherd

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†Deceased.

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Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

Clinical trial information: NCT00078949.

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0732-183X/14/3231w-3490w/$20.00

ABSTRACT

Purpose

For patients with relapsed or refractory aggressive lymphoma, we hypothesized that gemcitabine-based therapy before autologous stem-cell transplantation (ASCT) is as effective as and less toxic than standard treatment.

Patients and Methods

We randomly assigned 619 patients with relapsed/refractory aggressive lymphoma to treatment with gemcitabine, dexamethasone, and cisplatin (GDP) or to dexamethasone, cytarabine, and cisplatin (DHAP). Patients with B-cell lymphoma also received rituximab. Responding patients proceeded to stem-cell collection and ASCT. Coprimary end points were response rate after two treatment cycles and transplantation rate. The noninferiority margin for the response rate to GDP relative to DHAP was set at 10%. Secondary end points included event-free and overall survival, treatment toxicity, and quality of life.

Results

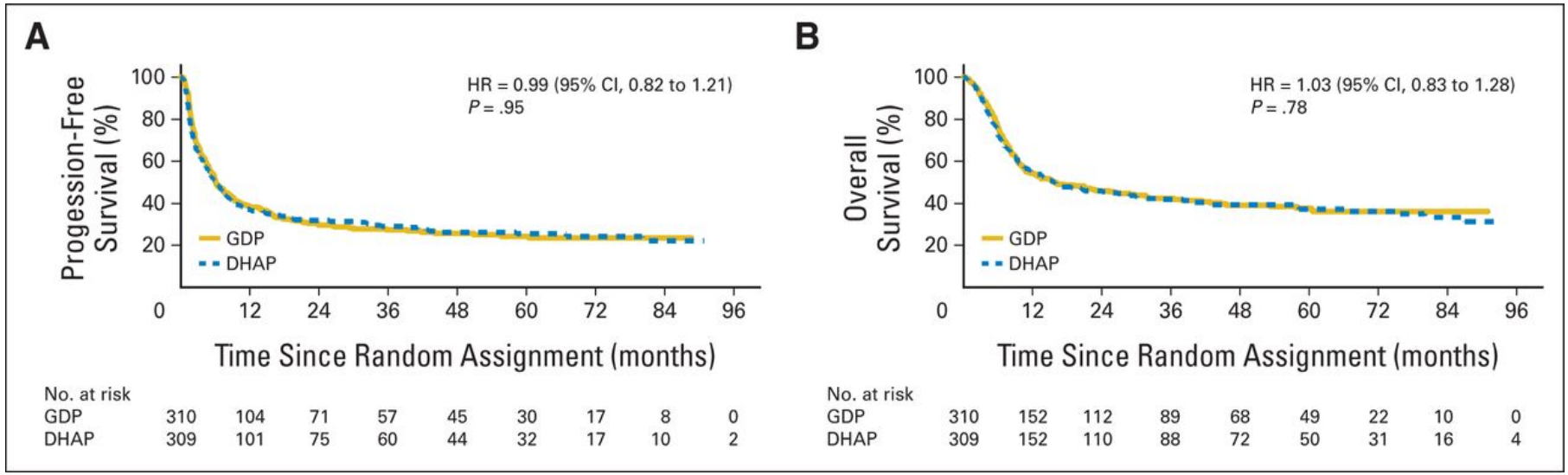
For the intention-to-treat population, the response rate with GDP was 45.2%; with DHAP the response rate was 44.0% (95% CI for difference, −9.0% to 6.7%), meeting protocol-defined criteria for noninferiority of GDP ($P = .005$). Similar results were obtained in a per-protocol analysis. The transplantation rates were 52.1% with GDP and 49.3% with DHAP ($P = .44$). At a median follow-up of 53 months, no differences were detected in event-free survival (HR, 0.99; stratified log-rank $P = .95$) or overall survival (HR, 1.03; $P = .78$) between GDP and DHAP. Treatment with GDP was associated with less toxicity ($P < .001$) and need for hospitalization ($P < .001$), and preserved quality of life ($P = .04$).

Conclusion

For patients with relapsed or refractory aggressive lymphoma, in comparison with DHAP, treatment with GDP is associated with a noninferior response rate, similar transplantation rate, event-free survival, and overall survival, less toxicity and hospitalization, and superior quality of life.

J Clin Oncol 32:3490-3496. © 2014 by American Society of Clinical Oncology

(A) Progression-free survival for patients randomly assigned to gemcitabine, dexamethasone, and cisplatin (GDP; gold line) or dexamethasone, cytarabine, and cisplatin (DHAP; blue dashed line)



Michael Crump et al. JCO 2014;32:3490-3496