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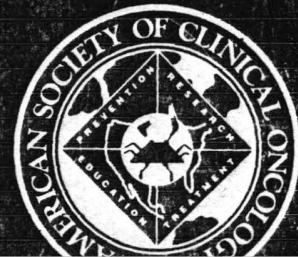
PROGRAM/PROCEEDINGS

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

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Thirty-Sixth Annual Meeting

May 20-23, 2000



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Thirty-Sixth
Annual Meeting of the
American Society of Clinical Oncology
May 20-23, 2000
New Orleans, Louisiana
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The *American Society of Clinical Oncology Program/Proceedings* (ISBN 0-9664495-4-1) is published by the American Society of Clinical Oncology, Alexandria, VA 22314. The 2000 issue is produced and printed by Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436.

Editorial correspondence and production questions should be addressed to *American Society of Clinical Oncology Program/Proceedings*, American Society of Clinical Oncology Publications Department, 850 Boylston Street, Chestnut Hill, MA 02467. Telephone: (617)739-8909. Fax: (617)739-8541. Email: ascopubs@asco.org.

Single issue rate, \$50.00. For all areas outside the United States and possessions, there is an additional charge for surface delivery of \$10.00. For airmail delivery, add \$15.00.

Prices are subject to change. Back volumes exist and are available at previous published prices. For further information, call (617)739-8909.

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Abstract management and indexing provided by Medical Support Systems, Cambridge, MA. Composition services and print production provided by Lippincott Williams & Wilkins, Baltimore, MD, and Cadmus Professional Services, Linthicum, MD.

Contents

Program and Proceedings Information	
<i>ASCO OnLine</i> (www.asco.org) Information	iv
ASCO Officers and Directors	v
Committee Rosters	vi
Session Descriptions	vii
Calendar of Events	ix
Highlight Sessions	
Opening Ceremony	xix
Plenary Session	xx
Integrated Symposium	xxi
Special Sessions	xxiii
Annual Business Meeting	xxix
Award Recipients	xxx
2000 ASCO Merit Awards	xxxix
2000 ASCO Travel Awards	xxxiii
General Information	xxxiv
ASCO Shuttle Service	xxxviii
Ernest N. Morial Convention Center Map	xl
2000 ASCO Exhibitor List	xli
2000 Annual Meeting Support	xlvi
ASCO Meeting Program	xlvi
2000 Abstracts	
Plenary Session	1a
Integrated Session	2a
Adult Leukemia and Lymphoma	4a
Bone Marrow Transplantation/Cytokines	47a
Breast Cancer	70a
Central Nervous System Tumors	158a
Clinical Pharmacology	175a
Gastrointestinal Cancer	238a
Genitourinary Cancer	326a
Gynecologic Cancer	378a
Head and Neck Cancer	411a
Health Services Research	433a
Immunobiology and Biologic Therapy	453a
Lung Cancer	482a
Melanoma and Sarcoma	550a
Pediatric Oncology	580a
Symptom Management	598a
Tumor Biology/Human Genetics	645a
Indexes	
Disclosure Index	669a
Author Index	696a
Subject Index	750a

109

True Thymic Hyperplasia (TTH) After Treatment of Adult Patients (Pts) with Non-Hodgkin's Lymphoma (NHL) and Hodgkin's Disease (HD). C. Chacon, N. Tartas, E. Domenichini, H. Pascuccelli, V. Sporn, J. Mazzucco, J. Korin, L. Barazzutti, H. Ferro, P. Busso, C. Foncuberta, G. Kusminsky, R. Chacon, J. Sanchez Avalos; Alexander Fleming Institute, Buenos Aires, Argentina; CEH, Buenos Aires, Argentina

Although thymic enlargement has been occasionally reported after chemotherapy (CHT) in young adults with HD and NHL, systematic studies including pathologic sampling of thymic RM have not been previously performed. We report here our experience in 8 pts treated for lymphoma who had thymic enlargement within twelve months of front line CHT. Six pts with HD and 2 pts with large cell lymphoma with sclerosis (DLC w/s) showed thymic enlargement on a computed tomography scan (CT) 2 to 12 months after therapy. Seven pts showed the typical sail image in the anterior superior mediastinal space, while 1 pt showed a cystic mass. These were all adult pts, with a median age of 25 yrs old (15-38). All pts were asymptomatic and in complete remission at the time of the study. It is relevant to say that only 3 pts had initially bulky disease. In addition to the CT scans, ^{67}Ga SPECT and MRI were performed in the 8 pts. The enlarged thymus was ^{67}Ga negative in all 8 pts. The MRI was inconclusive in 1, false positive in 3 and negative for lymphoma in the remainder. In 4 individuals a biopsy of the thymus was performed, 3/4 fulfilled the histologic criteria of true thymic hyperplasia (TTH). In 1 pt, a multilocular cystic thymus was excised. One patient with DLCL w/s had on the biopsy TTH plus hemorrhages and necrosis, interestingly this patient did not have bulky disease at presentation. The 8 pts are alive and in complete remission (CR) with a median follow up of 27 months (11-60). None of the pts developed other symptoms or signs of immune phenomena. TTH refers to an actual increase in thymic size, histologically has the appearance of normal thymus and should only have a minor component of adipose tissue, it is usually diagnosed with conventional radiologic studies. The results of CT scans, ^{67}Ga , MRI and histologic studies in this cohort of pts with TTH, were matched with clinical follow up. Contrarily to other reports a hyperplastic thymus has always been ^{67}Ga negative in our previous and present experience. MRI studies performed early after treatment might give false positive or inconclusive results. In conclusion we think that a residual mass in the superior anterior mediastinal space in a patient with lymphoma after treatment, might be due to TTH. These pts must not be empirically irradiated if they have a negative gallium scan.

111

Encouraging Improvement in Cytopenias of Patients with Myelodysplastic Syndromes (MDS) with Thalidomide. A. Raza, L. Lisak, C. Anderews, L. Little, F. Zorat, V. Shetty, S. Alvi, S. Mundle, K. Allampallam, M. duRant, M. Ekbal, M. Muzammil; Rush Cancer Institute, Chicago, IL; Rush-Presbyterian-St Luke's Medical Ctr, Chicago, IL

MDS patients present with variable cytopenias even though their bone marrows (BM) are generally hypercellular. Excessive cytokine-induced apoptosis of hematopoietic cells in the marrows has been proposed as a possible mechanism to explain the paucity of cells in the periphery. Tumor necrosis factor (TNF- α) is a pro-inflammatory cytokine which has been found in excessive amounts in MDS marrows. In addition, recent studies demonstrate excessive neo-angiogenesis in MDS marrows as well. TNF- α is a potent inducer of neo-angiogenesis via upregulation of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (b-FGF). A strategy for improving ineffective hematopoiesis in MDS would be directed at suppressing TNF- α and neo-angiogenesis. Thalidomide is active at both levels. We have treated 61 MDS patients with 100-400 mg thalidomide po h.s. for 12 weeks. Of these, 22 had refractory anemia (RA), 13 had RA with ringed sideroblasts (RARS), 19 had RA with excess blasts (RAEB), 4 had RAEB in transformation and 3 had CMMoL. Of 61 patients, 11 are off study, 25 are too early and 25 are evaluable for response, 17/25 are responding while 8/25 are not. Three have a trilineage, 4 bilineage and 10 monolineage responses. Most dramatic improvements are noted in erythroid series in that long-term transfusion dependent patients are becoming transfusion-independent. Responses can take up to 12 weeks to become apparent. Most patients tolerated the drug well in low doses (200 mg hs). We conclude that thalidomide in low doses given for prolonged periods to MDS patients can produce excellent palliation and deserves to be tested in a larger series of patients either alone or in combination with chemotherapy or anti-cytokine therapy.

110

Presence of Activation Markers of EBV and CMV in Myelodysplasia. S. Mundle, K. Allampallam, B. Y. Mativi, B. Dangerfield, J. Cartledge, S. Alvi, C. Shetty, S. Dar, E. Broderick, P. Vengopal, S. A. Gregory, A. Raza; Rush Cancer Institute, Chicago, IL; Rush-Presbyterian-St Luke's Medical Ctr, Chicago, IL

Herpes viruses have been known to establish latency in bone marrow (BM) early precursors such as a common precursor of dendritic and myeloid cells. The present studies were designed to examine if activation of these latent viruses occurs in myelodysplastic syndromes (MDS) as compared to normal marrows. Two herpes viruses, viz. Cytomegalovirus (CMV), and Epstein Barr Virus (EBV), commonly found latent in BM cells were investigated. First, BM aspirate mononuclear cells (BMMNC) from nineteen MDS patients were studied in comparison with 7 normal healthy donors. One MDS patient was studied on 2 occasions. Per FAB classification, 8 MDS cases were refractory anemia (RA), 1 RA with ringed sideroblasts (RARS), 3 RA with excess blasts (RAEB), 1 RAEB in transformation (RAEBt), 1 MDS \rightarrow AML, and 5 had chronic myelomonocytic leukemia (CMMoL). The expression of 2 m-RNA transcripts; at least one of them being indicative of virus activation, were examined for both CMV and EBV, using a reverse transcriptase polymerase chain reaction (RT-PCR). The specific primers for the Major Immediate Early Protein (IEP) and DNA Polymerase I (DNA-Pol) were selected for CMV, while for EBV, Latency related Membrane Protein 1 (LMP-1) and BZLF expression were assessed. All the MDS as well as the normal BM specimens showed the expression of latency related transcripts for the 2 viruses, IEP (Product-435bp) and LMP-1 (Product-106bp) respectively. In contrast, the expression of DNA-Pol (356bp) indicative of active CMV infection was rare both in MDS (2/19) and Normal (1/7) BMs. Interestingly, BZLF expression (608bp), indicative of active EBV, was evident in 10/19 MDS patients studied (>50%). Comparatively, only 2/7 normal BMs showed BZLF (~14%). Subsequently, long term stromal cultures were established from the BMs of MDS and normal individuals. At 75% confluency (~3-4weeks), they were overlaid with cord blood MNC (CMNC) and after coinoculation for one week RTPCR assays for EBV-BZLF and CMV-DNA Pol were performed on non adherent CMNC. Of the 3 CMNC specimens tested none showed these transcripts before overlaying, nor after coinoculation with normal stroma. Interestingly 1/3 CMMNC sample showed EBV-BZLF and CMV-DNA Pol m-RNA, albeit with stromal cultures from different patients. Thus, MDS stroma may be capable of activating herpes viruses and hematopoietic cells may show active herpes virus. Further studies are warranted to assess the association of herpes viruses with the pathobiology of MDS.

112

Outcome of Patients with Multiple Myeloma (MM) Receiving High-Dose Chemotherapy (HDC) and Hematopoietic Stem Cell Transplantation (HSCT). Z. Nahleh, K. Zimmerman, I. Tabbara; George Washington Univ Sch of Medicine, BMT Program, Washington, DC

Between 8/93 and 6/99, 14 patients with MM received HDC and HSCT. The preparative regimen consisted of either high-dose melphalan (200 mg/m²) in 6 patients or cyclophosphamide (120 mg/kg) and busulfan (16 mg/kg) in 8 patients. Half of the patients were male and the other half were females. The median time from diagnosis to transplant was 906 days (range 180-3600). The mean number of prior chemotherapy regimens was 2 (range 1-4). Four patients (28.5%) had stage I, 2 patients (14.2%) had stage II and 8 patients (57.1%) had stage III. IgG monoclonal spike was present in 10 patients, IgA monoclonal spike in 1 patient and 3 patients had light chain disease. At the time of transplant, 2 patients (14.2%) had refractory disease to VAD chemotherapy, 8 patients (57.1%) had achieved a PR and 4 patients (28.5%) were in CR. Following HDC and HSCT, 12 patients (85.7%) were in CR and 2 patients (14.2%) were in PR (1 patient had refractory disease and the other one was in PR.) The median progression-free survival (PFS) was 24.8 months (range 6-72 months.) Two patients died while in CR at 180 and 865 days post transplant from myocardial infarction and pneumonia respectively. Among patients who received Bu/Cy, the median time to ANC>500 was 11.5 days (9-18) and median time to platelet >20,000 was 14.4 days (7-38) as compared to 13 days (5-28) and 13.5 days (5-30) respectively for patients who received high-dose melphalan. The three patients who developed major toxicities (1 VOD and 2 hemorrhagic cystitis) received Bu/Cy. There was no treatment-related mortality. These data suggest that HDC and HSCT in MM is well tolerated with minimal toxicity and is associated with long-term PFS. In addition, high-dose melphalan is associated with less toxicity than Bu/Cy with comparable outcome.