MICHIGAN DEPARTMENT OF COMMUNITY HEALTH
BONE MARROW TRANSPLANTATION SERVICES
STANDARD ADVISORY COMMITTEE (BMTSAC) MEETING

Friday, August 28, 2009

Capitol View Building
201 Townsend Street
MDCH Conference Center
Lansing, Michigan 48913

APPROVED MINUTES

I. Call to Order

Chairperson VeCasey called the meeting to order at 9:11 a.m.

A. Members Present:

Paul Adams, MD, Vice-Chairperson, Self
Aly Abdel-Mageed, MD, Spectrum Health
Adil Akhtar, MD, Beaumont Hospitals
Thomas Ruane, MD, Blue Cross Blue Shield/Blue Care Network
Elna Saah, MD, Michigan State University (Left at 12:31 p.m.)
Samuel Silver, MD, University of Michigan Health System
Joseph Uberti, MD PhD, Barbara Ann Karmanos Cancer Institute
Amy Vanderwoude, MD, Cancer & Hematology Centers of West Michigan (arrived at 9:35 a.m.)
Donald VeCasey, Chairperson, Consumer Health Care Coalitiion
Michael Wiemann, MD FACP, St. John Health System (left at 10:50 a.m.)

B. Members Absent:

Grant Grace, UAW
Mary Marks, Alliance for Health
Jeffrey Trent, PhD, VanAndel Research Institute
Nalini Janakiraman, MD, Henry Ford Health System

C. Michigan Department of Community Health Staff Present:

Jessica Austin
Michael Berrios
Sallie Flanders
Kasi Kelley
Irma Lopez
Nick Lyon
Andrea Moore
Tania Rodriguez
Brenda Rogers

II. Declaration of Conflicts of Interests

No conflicts were noted for the record.

III. Review of Agenda

Motion by Dr. Ruane, seconded by Dr. Saah, to approve agenda as modified by adding a discussion on separate standards for autologous vs. allogeneic under item V.
Motion Carried.

IV. Review of Minutes July 29, 2009

Correction to Dr. Trent's title, and attendance at meeting. Title should be PhD, and he was absent.

Motion by Dr. Ruane, seconded by Dr. Uberti, to accept the minutes as modified.
Motion Carried.

V. Summary of SAC Activity & Review of Charge

Public Comment:
Bob Meeker, Spectrum Health

Chairperson VeCasey gave an overview of the SAC's activity and recommendations he will provide to the Commission on September 10, 2009.

Discussion followed.

Break at 10:28 a.m. – 10:49 a.m.

Dr. Wiemann gave an oral and written summary on rationale for increasing autologous stem cell transplant programs in Michigan. (Attachment A)

Discussion followed.

Public Comment:
Karen Kippen, Henry Ford Health System
Dennis McCafferty, Economic Alliance of Michigan
Patrick O'Donovan, Beaumont Hospital

VI. Discussion of Comparative Review Criteria

Dr. Abdel-Mageed will review the comparative review language as well as the project delivery requirements language and will bring back his suggestions to the September 24, 2009 meeting.

Public Comment:
Bob Meeker, Spectrum Health
Dennis McCafferty, Economic Alliance of Michigan

VII. Clarification of Cap for both Planning Areas

Motion by Dr. Abdel-Mageed, seconded by Dr. Ruane, to clarify the previous motion (July 29, 2009) to have three adult BMT programs on the east side of the state and one adult program on the west side of the state.
Motion Carried.

VIII. Discussion of Report to Commission for September 10, 2009 Meeting

Chairperson VeCasey discussed the three items of the charge that he was going to report to the CON Commission at the September 10, 2009 meeting. More specifically, continue regulation of BMT under CON, and there was determined to be both access and need issues in West Michigan. Additionally, he will report that there is consideration of splitting autologous and allogeneic transplant standards to allow for more autologous centers.

Discussion followed.

IX. Public Comment

Bob Meeker, Spectrum Health

X. Future Meeting Dates

September 24, 2009
October 22, 2009
November 18, 2009

XI. Next Steps

Dr. Abdel-Mageed will give a presentation on comparative review and project delivery requirements.

Dr. Wiemann will give a presentation for the consideration of two sets of standards; one for Allogeneic transplants and one for Autologous transplants.

XII. Future Meeting Dates

September 24, 2009
October 22, 2009
November 18, 2009

XIII. Adjournment

Motion by Dr. Abdel-Mageed, seconded by Dr. Ahktar, to adjourn the meeting at 12:35 p.m. Motion Carried.

Rationale for Increasing Autologous Stem Cell Transplant Programs in Michigan

Introduction:

Currently the number of Bone Marrow Transplant (more properly termed Stem Cell Transplant {SCT} given today's technologies) programs is regulated by the State of Michigan Certificate of Need process, and is limited to three for adults and four for children. The CON standards have not remained current with the technology that is now common place whereby autologous SCT is the more prevalent form of transplantation, nationally is considered the standard of care in a community setting, and represents more cost effective and curative treatment than newer drug therapy regimens. At least three states have Autologous specific CON standards (North Carolina, Maryland, and Florida) with the volume requirements in these states ranging from ten to twenty procedures. Both St. John Health System and William Beaumont Hospitals believes autologous SCT should not be regulated by Michigan CON standards, but if regulated, standards should be institution specific and tied to national accrediting body required qualifications.

Rationale Summary:

1. **Costs** associated with alternative therapies to SCT are more expensive than the SCT procedure and follow-up treatment.
2. **Quality** related to SCT programs and practitioners is determined and monitored by a well-regarded accrediting body, the Foundation for the Accreditation of Hematopoietic Cellular Therapy (FAHCT).
3. **Access** to SCT should be made available at community cancer centers where earlier treatment of cancer patients has shown to improve survival rates.

Rationale Details: Costs

- St. Vincent Hospitals and Health Services (Indianapolis, IN) provided 24 patients with BMT services during a recent 12-month period at an average cost of $43,646[i]

  This cornpares favorably with other treatments:
  - Imatinib (3-5 year treatment) $90,000-$150,000[ii]
  - R-hyper CVAD $32,000 plus costs associated with a 36 day inpatient stay.[iii]
- **Cost of hematopoietic growth factors:**
  - These are drugs that stimulate production of red blood cells (Procrit or Aranesp) or granulocytes (granulocyte colony stimulating factor [G-CSF] like Neupogen or Neulasta). Like many new drugs in Oncology, they are very expensive. A 10 day course of neupogen (or one injection of Neulasta) costs > $2000. They are often used after each cycle of standard cytotoxic chemotherapy hence increasing the overall cost. In one study, G-CSF was used in conjunction with induction chemotherapy for elderly patients with acute myelogenous leukemia (AML) in a randomized trial.[iv] Results showed that G-CSF had 'some clinical benefits but did not reduce the duration of hospitalization, prolong survival or reduce the overall cost of supportive care'. The cost of induction therapy with G-CSF was $50,593. In best case-scenario, patients who achieve complete remission with first cycle of induction chemotherapy will undergo at least 2 additional

cycles of 'consolidation'. The total cost of chemotherapy for AML is, therefore no less than SCT.

- **Cost R-hyper CVAD regimen for the treatment of Mantle Cell Lymphoma (MCL):**
  - This regimen is considered standard of care for MCL, it consist of combination of cytotoxic chemotherapy (with recent addition of Rituximab) given in 2 blocks, A and B alternating every 3 weeks. A full course of therapy involves total of 8 treatments (4 A and 4 B).[v] All therapy is done as inpatient. Part A requires hospital stay for a minimum of 4 days and Part B requires average inpatient stay of 5 days. Total inpatient days for therapy without any complications or re-admissions is (4x4)=16 days for part A + (5x4)=20 for part B; total =36 days which is more than average hospital stay for a transplant patient. If one adds the cost of rituximab ($4000 per cycle) which is now used in conjunction with this regimen plus use of growth factors (G-CSF) and re-admissions for complications, the actual cost of this regimen exceeds that of SCT.

At the same time that cost of standard therapy, as alternative to SCT, has continued to increase as a result of incorporating newer, more expensive drugs, the cost of SCT had come down considerably. Example of cost of SCT is shown below:

- Peripheral blood stem cell transplant (PBSCT) in patients with relapsed lymphoma results in accelerated reconstitution, improved quality of life and cost reduction compared with bone marrow transplantation (BMT).[vi] This study was done in the Netherlands and cost was calculated in US dollars. The study concluded that: 'Total transplantation costs were significantly lower in the PSCT arm [$13,954 ($4913- 29,532) versus $17 668 ($10,170-44,083) $P < 0.05$], as a result of the reduced hospital stay and lower antibiotic costs. In summary, these results indicate that PSCT is superior to ABMT with regard to engraftment, supportive care, quality of life and cost.'

Rationale Details: Quality

- **The 100-day mortality rates after autologous transplantation are lower than that for allogeneic.**[v]

- **Autologous BMT which offers the opportunity for earlier treatment can lead to an increased probability of survival.** [v]

- **Peripheral blood stem cells can be harvested, cryopreserved, and infused safely in an outpatient setting.** [vi]
- **Resources for care of patients receiving HDC with PBSC support are available in community cancer centers.** [vi]
  - With an appropriate infrastructure, practicing oncologists who treat patients with intensive chemotherapy already have the skills necessary to manage patients receiving high-dose chemotherapy (HDC) with peripheral blood stem cell (PBSC) support.
  - The care of patients receiving well-tested HDC regimens with PBSC support is generally no more complex than that of patients with acute myeloid leukemia (AML) through multiple cycles of induction and

consolidation. Oncologists who routinely manage patients with AML are caring for patients who receive very toxic regimens with resultant prolonged pancytopenia and severe and often fatal complications. Care of patients with AML requires sophisticated transfusion services and availability of consultants who can also be utilized for the care of patients receiving HDC.

- **HDC can be administered without prohibitive morbidity and mortality in an outpatient setting in community cancer centers.** [vi]

Treatment-related mortality in the first 100 days following HDC and PBSC support in community cancer centers

Reference	*n*	Regimen	Disease	Phase	TRM
[29]	1,000	Varied	Varied	Varied	3.4%
[24, 30-32]	208	BEAC	Malignant lymphoma	Relapsed	3.6%-10%
[33]	55	Mel x2	Multiple myeloma	Newly Diagnosed	5%
[34]	93	CTCb	Breast cancer	Metastatic, new	0%
[35]	95	CTCb	Breast cancer	Stage II-III	0%
[36]	315	CTCb	Breast cancer	Stage II-III	0.3%
[37]	29	MMC	Ovarian cancer	Relapsed	6.9%

BEAC = carmustine, etoposide, cytarabine and cyclophosphamide; Mel = melphalan; CTCb= cyclophosphamide, thiotepa and carboplatin MMC = melphalan, mitoxantrone, and carboplatin; TRM = treatment-related mortality

- **Neutrophil and platelet recovery is rapid and complete following infusion of adequate quantities of PBSC as measured by CD34 cells.** [vi]
  - With the use of PBSC, larger quantities of stem cells and progenitors can be collected, resulting in more rapid recovery of neutrophils and platelets, with virtually all patients recovering blood counts within two weeks. This short period of pancytopenia has significantly lowered the cost of performing HDC by allowing much of the treatment to take place in an outpatient setting where patients are carefully monitored and receive prophylactic antibiotics and platelet transfusions.
- **Outcomes of patients treated in community cancer centers are comparable to results reported in the literature from transplant centers.** [vi]

Results of clinical trials of HDC and autologous PBSC infusion in community cancer centers

Reference	*n*	Disease	Phase	OS %	EFS %	Time (months)
[32]	83	NHL, high and inter.	Relapse	48	38	36
[31]	49	NHL, low-grade	Relapse	58	36	43
[30]	28	Hodgkin's disease	Relapse	77	64	36
[33]	55	Multiple Myeloma	Early	84	76	18
[34]	93	Breast cancer	Metastatic	42	19	42
[35]	96	Breast cancer	II-III, ≥ 10 + nodes	77	61	48
[46]	48	Breast cancer	II-III, > 5-9 + nodes	77	67	48
[37]	31	Ovarian cancer	Advanced relapse	60	30	18

OS = overall survival; EFS = event-free survival; Time = time of estimate of probablity of OS or EPS; II-III = stage of disease

Rationale Details: Access

- **"Limited stem cell availability" – Not so with autologous.**
- **Autologous transplantation is substantially better than chemotherapy for treating the first relapse of large-cell non-Hodgkin's lymphoma that is sensitive to chemotherapy.**[vii]
- **Data from the National Cancer Institute suggests that ony a minority of patients with a relapse responsive to chemotherapy ever undergo autologous transplantation.**[vii]
- **Patients most likely to benefit from HDC could be treated earlier in the natural history of their diseases if such therapy were available to the practicing oncologists.** [vi]
    - Outcomes for patients receiving HDC are better if the therapy is applied early in the disease course before resistance develops.
- **Family and social support systems remain intact.** [vi]
    - When the patient is treated in the community where he or she lives, the support system remains intact. Patients treated at a tertiary transplant center are also required to have a full-time caregiver with them throughout treatment which can create hardships on family and friends.
- **Expense of living away from home can be avoided.** [vi]
    - In addition to the social disruption of being treated away from home, the nonmedical economic costs can be great, especially when the primary caregiver is also the primary wage earner.
- **Access to clinical trials is improved.** [vi]
    - For practical purposes, patients who cannot afford the social or economic dislocation that treatment in a transplant center entails are essentially denied access to clinical care of greater curative potential and clinical trials participation.
- **There are not enough transplant centers in the U.S. to perform indicated HDC treatments or necessary clinical trials.** [vi]
    - Only 10%-15% of patients under the age of 65 with NHL who fail chemotherapy receive HDC with it curative potential. One reason for this is the current relative unavailability of this technology in the community.
- **There is potential cost savings in transferring of PBSC technology to the community.** [vi]
    - Community cancer centers enjoy a lower fixed cost structure and should be able to deliver HDC with PBSC support at case rates lower than those required by academic centers who have the expense of research and education with a commensurately large overhead.

References

[i] St. Vincent Hospitals and Health Services, Indianapolis, IN

[ii] John Goldman. Is imatinib a cost-effective treatment for newly diagnosed chronic myeloid leukemia patients? Nature Clinical Practice Oncology (2005) 2, 126-127

[iii] CCO Formulary October 2005

[iv] CL. Bennett , D. Hynes , J. Godwin , TJ. Stinson , RM. Golub , FR. Appelbaum; Southwest Oncology Group. Economic analysis of granulocyte colony stimulating factor as adjunct therapy for older patients with acute myelogenous leukemia (AML): estimates from a Southwest Oncology Group clinical trial. Cancer Invest 2001;19(6):603-10

[v] CCO Formulary October 2005

[vi] Department of Haematology, University Hospital Groningen, The Netherlands. Autologous peripheral blood stem cell transplantation in patients with relapsed lymphoma results in accelerated haematopoietic reconstitution, improved quality of life and cost reduction compared with bone marrow transplantation: the Hovon 22 study. Br J Haematol 2001, 114(2):319-26

[v] Karmanos Cancer Institute. Bone Marrow Transplant CON Standards July 29, 2009

vi C.H. Weaver, W. West, L. Schwartzberg, R. Birch and C.D. Buckner. The Rationale for Performing Autologous Peripheral Blood Stem Cell Transplants in Community Cancer Centers. The Oncologist 1998;3;346-353

vii Edward A. Copelan, M.D. Hematopoietic Stem-Cell Transplantation. The New England Journal of Medicine 354:17 April 27, 2006