Hematopoietic Stem cell transplantation and solid tumors

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Hematology Department, Head
Background

- For more than forty years, allogeneic hematopoietic stem cell transplants (HSCT) have been used to treat malignancies.
- Allo HSCT is potentially curative for CML, AML, ALL, NHL, and Hodgkin’s disease.
- Because of Allo-HSCT success in treating hematologic malignancies,
  - Autologous HSCT has been considered
  - Interest in solid tumors has raised.
Hematopoetic Stem Cell Transplant

- **Autologous HSCT: Graft from the patient**
  - The idea: to allow Hematological recovery after HD Chemotherapy
  - The active treatment = HD Chemotherapy

- **Allogeneic HSCT: Graft from a Donor**
  - The idea: To transfer a new immune system to a patient with Cancer
  - The active treatment = Transplant
Rational for Auto HSCT in ST

• Most solid tumors are at least moderately responsive to cytotoxic chemotherapy.
• Most chemotherapeutic agents show a steep dose-response curve
  – This led to the concept of dose intensity, expressed as average dose per week over the course of treatment
    • Regional therapy
    • HDCT
• Unfortunately, there is a limit to how much the dose of chemotherapy medication may be increased due to the toxicity of the treatment.
    • HDCT

Modified from Kuperman et from JP Lotz
High-Dose Chemotherapy: Rationale

No. Cycles

Cumulative dose  DI

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Courtesy from JP Lotz
Autologous HSCT for Solid Tumors

• Low malignant cell contamination as compared to Leukemia

• Favored by technical changes
  – Bone Marrow vs. PBSC harvest
Bone Marrow Harvest
Peripheral Blood Stem Cell Harvest
Autologous HSCT for Solid Tumors

• Low malignant cell contamination as compared to Leukemia
• Favored by technical changes
  – Bone Marrow vs. PBSC harvest
• Large number of patients for some diseases
  – Breast
Hematopoetic stem cell transplantation for solid tumors in Europe

A. Gratwohl¹, H. Baldomero¹, T. Demirer², G. Rosti³, G. Dini⁴, R. Ladenstein⁵ & A. Urbano-Ispizua⁶
On behalf of the Accreditation Committee of the European Group for Blood and Marrow Transplantation (EBMT) in cooperation with the Working Party on Solid Tumours (STWP) and the Working Party on Pediatric Diseases (PDWP)
Design of HDCT

Up-front (Bezwoda)

Standard followed by HDCT (Ayash, Somlo, Lotz)

Sequential HDCT (Crown, Ayash)
Design of HDCT

- Tandem (Wallerstein, Lotz)
- Delayed HDCT (Peters)
- HD followed by SD CT (Tallman)

29/11/2007
Novi Sad
<table>
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<tr>
<th>Disease Indication</th>
<th>Mean TR</th>
<th>SD</th>
<th>CV</th>
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ALLO IN SOLID TUMORS
REASONS FOR INVESTIGATION?

- Not all patients are cured with present TRT
  - chemo / HD chemo
  - Cytokines / New drugs
    - Young and active patients

- Allo BMT is an efficient tool to control leukemias
Donor for allogeneic HSCT

- Intrafamilial Donor
  - HLA compatible
    - HLA Matched related sibling
    - Monozygote twin
  - Partially matched transplant: Haplo

- Non Familial Donor/graft
  - HLA compatible : MUD
  - Partially HLA compatible
    - MMUD
    - Cord Blood
ASCT for SOLID TUMORS

- Thomas, 1956: Ovarian Carcinoma: N=1
- Matthay, 1994: Neuroblastoma: N=20
- Ben Yosef, 1996: Breast Ca. N=1

Evidence for a Graft-Versus-Tumor Effect in a Patient Treated With Marrow Ablative Chemotherapy and Allogeneic Bone Marrow Transplantation for Breast Cancer

By Brigitte Eibl, Hubert Schwaighofer, David Nachbaur, Christian Marth, Anne Gächter, Rudolf Knapp, Günther Böck, Christoph Gassner, Lothar Schiller, Finn Petersen, and Dietger Niederwieser

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<td>% Increase/decrease during 2004–2009</td>
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<td>55</td>
<td>51</td>
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<td>756</td>
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DISEASE

Date of diagnosis: 

yyyy  mm  dd

**PRIMARY DISEASE DIAGNOSIS** *(CHECK THE DISEASE FOR WHICH THIS TRANSPLANT WAS PERFORMED)*

- Acute Leukaemia
  - Myelogenous (AML)
  - Lymphoblastic (ALL)
- Secondary Acute Leukaemia *(do not use if transformed from MDS/MPN)*
- Chronic Leukaemia
  - Chronic Myeloid Leukaemia (CML)
  - Chronic Lymphocytic Leukaemia
- Lymphoma
  - Non Hodgkin
  - Hodgkin's Disease
- Other diagnosis, specify: ____________________________

- Myeloma /Plasma cell disorder
- Solid Tumour
- Myelodysplastic syndromes
  - MDS
  - MD/MPN
- Myeloproliferative neoplasm
- Bone marrow failure including Aplastic anaemia
- Inherited disorders
  - Primary immune deficiencies
  - Metabolic disorders

- Histiocytic disorders
- Autoimmune disease
  - Juvenile Idiopathic Arthritis
  - Multiple Sclerosis
  - Systemic Lupus
  - Systemic Sclerosis
- Haemoglobinopathy
### INITIAL DIAGNOSIS

- Bone sarcoma (excluding Ewing sarcoma/PNET)
- Central nervous system tumors (include CNS PNET)
- Colorectal
- Ewing sarcoma/PNET, extra-skeletal
- Ewing sarcoma/PNET, skeletal
- Germ cell tumour, extragonadal only
- Hepatobiliary
- Lung cancer, non-small cell
- Lung cancer, small cell
- Medulloblastoma
- Melanoma
- Other, specify

- Breast
- Neuroblastoma
- Ovarian
- Pancreas
- Prostate
- Renal cell
- Retinoblastoma
- Rhabdomyosarcoma
- Soft tissue sarcoma
- Testicular
- Thymoma
- Wilms tumour

**Histological grading:**  ........ (1 to 4)  
- Not evaluated
- Unknown

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<th>2</th>
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<th>4</th>
<th>X</th>
<th>Not evaluated</th>
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*For metastases, 0 indicates "No metastasis", 1 indicates "Metastasis" and X indicates "Not evaluable"

**OR**

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<th>Disease-specific staging</th>
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</table>
BREAST CARCINOMA ONLY

- Inflammatory □ Non-inflammatory □

RECEPTOR STATUS

- Estrogen (ER):
  - Negative □ Not evaluated □ Positive: Values □ Not evaluated □ Unknown
  - Not evaluated □ Unknown

- Progesterone (PgR):
  - Negative □ Not evaluated □ Positive: Values □ Not evaluated □ Unknown
  - Not evaluated □ Unknown

- HER2/neu (c-erb-B2):
  - Negative □ Not evaluated □ Positive: Defined by IHC 3+
    - IHC 2+ and FISH + □ Unknown
  - Not evaluated □ Unknown

HISTOLOGICAL SUBCLASSIFICATION FOR BREAST CARCINOMA

- Axillary lymph nodes: N° positive / N° examined = □ Not evaluated

  S.B.R. (Scarff-Bloom-Richardson)
  1 □ 2 □ 3 □ Not evaluated □ Unknown

- Ductal carcinoma
  - Yes □ No □ Not evaluated □ Unknown

- Lobular carcinoma
  - Yes □ No □ Not evaluated □ Unknown
Conclusions

- Autologous HSCT
  - Good way to deliver intensive chemotherapy
  - Is not the sole answer
  - New targeted drugs to be associated

- Allogeneic HSCT
  - Immunotherapy
  - Field not investigated

- But, Patients still died from solid tumors...