INNOVATION IN SCT

Gianantonio.rosti@unibo.it
The 1940s

The atomic bomb precipitated research leading to stem cell transplantation.
Clinical Stem Cell Transplantation and the beginnings of HLA typing

- 1957-Thomas
  - Safe infusion of marrow into humans
- 1959-Mathé
  - First bone marrow transplants for radiation accident victims.
- 1958-Dausset
  - First HLA antigen described (A2)
- 1963-Mathé
  - First successful complete engraftment and survival of over 1 year, description of acute and chronic GVHD in men
- 1968-van Rood/Terasaki
  - Modern HLA serologic typing available
  - Secondary disease-running syndrome-GVHD
- 1968-Good (Minneapolis) De Vries (Leiden)
  - First successful HLA-matched sibling transplant for SCID
Chronic myeloid leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

A. Hochhaus¹, S. Saussele², G. Rosti³, F.-X. Mahon⁴, J. J. W. M. Janssen⁵, H. Hjorth-Hansen⁶, J. Richter⁷ & C. Buske⁸, on behalf of the ESMO Guidelines Committee*
Allogeneic stem cell transplantation

The number of patients undergoing alloSCT for CML CP has decreased significantly since TKIs were introduced. AlloSCT remains an important therapeutic option for patients in CML CP who fail at least 2 TKIs or are potentially harbouring the T315I mutation (after a trial of ponatinib therapy) [V, B]. Patients at high risk for transformation should be considered for alloSCT, since outcome of alloSCT after transformation is unfavourable. Patients referred to transplant may have a better outcome if entering the transplant with a better response (lower CML burden). Assessment of donor availability will be prerequisite to achieve this goal.
Trends in Transplants by Transplant Type and Recipient Age* 1990-2010

* Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
Trends in Transplants by Type and Recipient Age* 2001-2010

* Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma

Transplants, %

- <=20 yrs
- 21-40 yrs
- 41-50 yrs
- 51-60 yrs
- >60 yrs

2001-2005
2006-2010

Allogeneic Transplants

Autologous Transplants
Trends in Allogeneic HCT in the US by Recipient Age

Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma
INDICATIONS FOR BLOOD AND MARROW TRANSPLANTATION (BMT) IN NORTH AMERICA 2002 (IBMTR)

Around 10% of allogeneic transplant done for CML
Indications for Hematopoietic Stem Cell Transplants in the United States, 2010
(Inflation factor: Auto=1.25 (80%), Allo=1.05 (95%), All Transplants)

- Around 3-4% of allogeneic transplant done for CML

Bar chart showing the number of transplants by indication and type:
- Multiple Myeloma: Allogeneic (Total N=8,860)
- NHL: Autologous (Total N=9,026)
- AML
- ALL
- MDS/MPD
- HD
- CML
- Aplastic Anemia
- Other Leuk
- Non-Malignant Disease
- Other Cancer

CIBMTR
Indications for Hematopoietic Cell Transplant in the US, 2017

- Allogeneic (Total N=8,780)
- Autologous (Total N=14,599)

Number of Transplants

Myeloma / PCD
NHL
AML
MDS / MPN
ALL
HD
Other Cancer
Other Non-Malignant Disease
Aplastic Anemia
CML
CLL
Probability of Survival after HLA-identical Sibling Donor Transplants for CML, 1998-2010
- By Disease Status and Transplant Year -

Probability of Survival, %

CP, 1998-2000 (N=2,239)
AP, 1998-2000 (N=291)
CP, 2001-2010 (N=2,498)
AP, 2001-2010 (N=360)

P < 0.0001

Years

0 1 2 3 4 5 6
0 10 20 30 40 50 60 70 80 90 100

CIBMTR®
Survival after HLA Matched Sibling HCT for CML, 2006-2016

- Chronic Phase (n=1,445)
- Accelerated Phase (n=221)
- Blast Phase (n=151)

p<0.001
100-day Mortality after HLA-identical Sibling Transplants, 2010

- Early Disease
- Intermediate Disease
- Advanced Disease
- Chronic Phase
- Accelerated Phase
- Blast Phase
- Other

Mortality, %

AML
ALL
CML
MDS/MPS
Aplastic Anemia
Immune Deficiency

CIBMTR®
Causes of Death after Transplants Done in 2009-2010

Unrelated Donor
- Primary Disease (37%)
- New Malignancy (1%)
- GVHD (18%)
- Infection (18%)
- Other (18%)
- Organ Failure (8%)

Autologous
- Primary Disease (72%)
- New Malignancy (1%)
- Infection (7%)
- Organ Failure (3%)
- Other (17%)

HLA-identical Sibling
- Primary Disease (49%)
- New Malignancy (1%)
- GVHD (16%)
- Infection (13%)
- Other (16%)
- Organ Failure (5%)

CIBMTR®
Slide 18
Causes of Death after HLA-Matched Sibling HCT done in 2015-2016

Died within 100 days post-transplant

- Primary Disease: 29%
- Infection: 19%
- Organ Failure: 8%
- GVHD: 11%
- Graft Rejection: 11%
- Hemorrhage: 1%
- Other: 1%

Died at or beyond 100 days post-transplant*

- Primary Disease: 57%
- Infection: 10%
- Organ Failure: 1%
- GVHD: 1%
- Graft Rejection: 1%
- Hemorrhage: 11%
- Second Malignancy: 8%
- Other: 1%

*Data reflects 3-year mortality

CIBMTR
Center for International Blood & Marrow Transplant Research
OS in CML 449 patients < 30 years old transplanted in early disease (CP1), by donor type and stem cell source.

LFS in 449 CML patients < 30 years old transplanted in early disease (CP1), by donor type and stem cell source.
Related and unrelated SCT meet less than half the need for donors

<table>
<thead>
<tr>
<th>Percentage of patients needing donors</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>21,000 no unrelated donor</td>
</tr>
<tr>
<td>42%</td>
<td>4,000 unrelated</td>
</tr>
<tr>
<td>30%</td>
<td>11,000 related</td>
</tr>
</tbody>
</table>

CBT, Haplo transplant
Allogeneic HCT Recipients in the US, by Donor Type

- URD-BM / PB
- HLA-identical Sib
- Other Relative
- URD / UCB

Number of Transplants


CIBMTR CENTER FOR INTERNATIONAL BLOOD & MARROW TRANSPLANT RESEARCH
ALLOGENEIC STEM CELL TRANSPLANTATION IN CML, STATE OF THE ART, 2019

BASELINE : NEVER

SECOND-LINE : “ALWAYS” IN BLAST PHASE,
             irrespective of the response to TKIs
             : “ALWAYS” IN ACCELERATED PHASE,
             if the response to the TKI is less than optimal
             : “NEVER” IN CHRONIC PHASE

THIRD-LINE : “ALWAYS” if the response to second-line TKI is
              less than optimal

THE VALUE AND THE MEANING OF “ALWAYS” DEPEND ON AGE,
COMORBIDITIES, PERFORMANCE STATUS, DONOR, etc. that is to say
ON TRANSPLANT RISK
Survival after HLA Matched Sibling HCT for CML, 2006-2016

- Chronic Phase (n=1,445)
- Accelerated Phase (n=221)
- Blast Phase (n=151)

p < 0.001